stray leaves and some fruit on cancer,
based upon physiologic chemical principles.

By

H. D. McCulloch,
M.D.

1907.

CONSIDER
WHENCE EACH THING
IS COME & OF WHAT
IT CONSISTS & INTO
WHAT IT CHANGES.

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ERRATA.

Page 3, line 20—for ‘ they permit . . . ’ read, ‘ this arrangement permits of a flow of fluids from the periphery to the nuclear membrane beyond which these lines do not penetrate, so that the cell may be suited to its especial environments by adaptation.’

Page 4, Fig. 3—for ‘ Rauvier ’ read ‘ Ranvier.’

Page 5, line 15—after the word ‘ unsymmetrical ’ mark (?) ; also whereever the name ‘ Delamere ’ occurs read ‘ Delamare.’

Page 23, line 20—for ‘ emperical ’ read ‘ empirical.’

Page 30—First line under ‘ Case V.’ read ‘ was admitted suffering from . . . .’

Page 43—First line ‘ parcisis ’ should read ‘ paresis.’

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Stray Leaves, and Some Fruit

ON

Cancer and Tuberculosis

Based upon physiologic chemical principles

BEING A

Thesis in Two Parts

(Illustrated with Diagrams and Chart)

BY

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PART I.

On the rôle of the Leucocyte in the natural production of specific vaccines in Cancer, Tuberculosis and other INFECTIONS, and their bearing on METASTASIS.

NOTWITHSTANDING the fact that hardly a single morbid condition is met with in which the lymphatic system and its glands are not more or less involved, the present-day practitioner cannot but be impressed with the singular lack of knowledge concerning the anatomical evolution or the physiological functions of the lymphatic systems and of the glands belonging to these systems. The nature of their action seems to have been so little understood, that they have been usually regarded as "the weak spots" in the anatomy of the organism. "The physician or surgeon is apt to under-estimate the power of resistance of lymphatic glands. because, in the nature of things, he is a witness only of their lost battles; those which they win remain unknown. That the victories are more frequent than we are in the habit of realizing is well illustrated by some observations of Manfredi."[1] Nevertheless when these systems have once been reached by the micro-organisms of a bacterial infection, they are supposed to find in them congenial soil. Eminent bacteriologists have spoken of the micro-organisms as "entrenching themselves with spindle cells" in the sub-mucous connective tissues; "and again such organisms on entering a cell might stimulate it to division, at the same time frequently dividing themselves, so that in each daughter cell would be a small colony of the micro-organisms." These glands are further supposed to provide for the subsequent proliferation of organisms, and a "nidus" or "focus" for the spreading of the infection; and this is said to be effected by way of the lymphatic ducts and channels.

The stages of swelling, degeneration, suppuration and caseation, that these glands are known to pass through, have tended to confirm this belief; and their extirpation, along with their adnexæ, has been therefore considered essential by the surgeon, before complete recovery from the disease can be hoped for.

Their dissection necessarily becomes a very lengthy, elaborate, and as a rule, incomplete procedure. Owing to the apparent unsymmetrical, intricate, and delicate inter-relationship of these glands with one another, and with the intercellular spaces in various parts of the body, which have never been, and are never likely to be, mapped out with sufficient anatomical precision, accurate surgical procedure is impossible. A complete extirpation of these structures, to include the "causa causans" and, at the same time, a certain wide margin of healthy tissue, can only, therefore, be conscientiously hoped for (as in cancer) at such an early stage of the disease that the individual concerned is hardly aware of any evidence of its presence. In ninety-nine cases out of a hundred what happens is, that medical attention is sought when, pathologically speaking, the disease is more extensive than appears to the naked eye of the patient, or the microscopically aided eye of the bacteriologist. Unfortunately, we have no means at hand for bringing the microscope to bear on the diseased site in the living tissues, until a portion of the suspected tissue is placed on the stage of the microscope; and, even then, unless the particular micro-organism can be detected and identified, it is difficult to conclude with certainty, where the physiological phenomena end and the pathological phenomena begin. For obvious reasons it is impossible to estimate either the epoch at which the stimuli producing the condition first occur, or the precise nature of the exciting cause. Profound changes are likely to have ensued at two points at least, namely, at the site of the stimulus on the one hand, and in the nearest correlated lymphatic gland on the other. In this reference the remarks of Dr. Mitchell Stevens are very suggestive, accounting for what he has well termed the "latent period."[2] The timely extirpation with the knife of the entire tissues, within a certain radius, is doubtless a perfect operation, with a perfect result. But, as has been stated, it is the great exception for the surgeon to opportunely meet with and diagnose such a case with certainty; and, in consequence of imperfect physiological reactions *in situ*, the disease becomes established, and extends in different directions; from these it is not possible to eradicate it with any certainty by a single operation or even by repeated surgical procedures. The resulting disease is now looked upon as a foreign monstrosity; hence the medieval terms Cancer, Lupus, etc. An eminent surgeon has recently gone so far as to attribute to the former of these diseases definite vascular organs. As he says:—"It is obvious that a living organism such as a cancer is, must conform to physiological rules, and that its products must escape by its veins or by its lymphatics."[3]

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[1] Encyclo. Medica.

The questions arise:—

(1). What is the origin and the rôle of the lymphatic systems in infections?

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[2] British Medical Journal. 9th Feb., 1907.

[3] British Medical Journal. Jan. 27th, 1906. P. 182.

(2). Where do the leucocytes which are concerned in a leucocytosis come from, in response to these unwonted stimuli ?

(3). If they perform phagocytosis, what becomes of the satiated phagocytes and their contents ?

(4). What becomes of those that are surfeited ? and

(5). What is the ultimate aim and object of phagocytosis ?

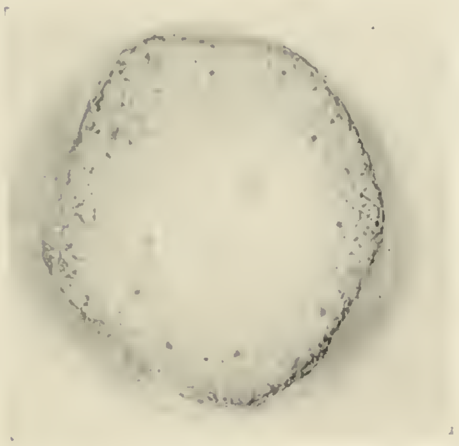
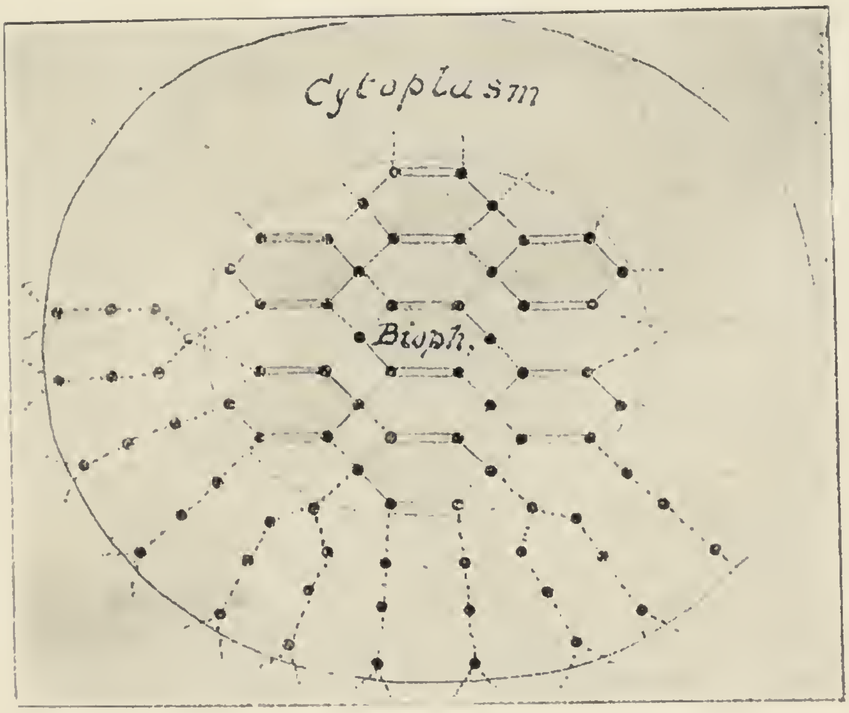


FIG. 1.—(a) Human leucocyte, anatomically mature and normal, showing details of structure previous to Mitosis. For stereoscopic effect, view through pin-hole in thin card.

I will endeavour to answer these questions hypothetically but categorically. I must therefore beg the indulgence of my readers. But, before doing so, a few remarks on the origin and the anatomy of these lymphatic glands may not be out of place.

The earliest indications of the lymphatic system that we have may be seen in the cytoplasm of the mature leucocyte itself. This is evidenced by the filamental reticulum which first appears in the peripheral parts of the cell, converging by irregular centripetal lines towards the nucleus, they permit of a flow of fluid from the periphery to the nuclear membrane, beyond which they do not penetrate, to suit the cell to its especial environment by adaptation.

These filamental channels become re-inforced later on by what are known as plasmosomes or zymogen granules. These are distributed un-symmetrically throughout the cytoplasm of the cell, but paravascu-



(b) Diagram of leucocyte (after Adami) illustrating 'skeletal' structure in regard to nuclear and cytoplasmic parts. Where nucleus represents germinatival and controlling centre and cytoplasm represents sensory, motor, circulatory, alimentative, digestive and excretory mechanisms.

larly to these channels, in their bifurcations or angles. These granules Professor Adami has indicated as originating from the nucleus itself. Their function is to produce the cell enzyme or cytase, which has been described as an extremely complex nucleo-proteid substance. These channels and plasmosomes represent respectively the lymphatic vessels and glands; and it is possible that Mr. Lockwood had them in mind when he spoke of the veins and lymphatics of the living organism of cancer.

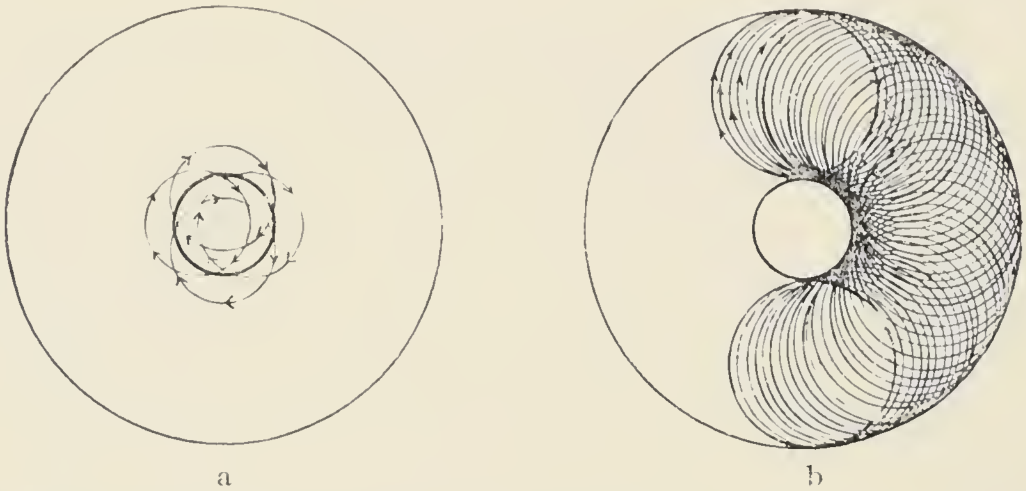


FIG. 2.—Illustrating leucocytic function. Metabolism. Repulsion to like bodies and affinity for unlike bodies. (a) Chemiotaxis—intra-nuclear. (b) Chemiotasis—internuclear and cyto-plasmic.

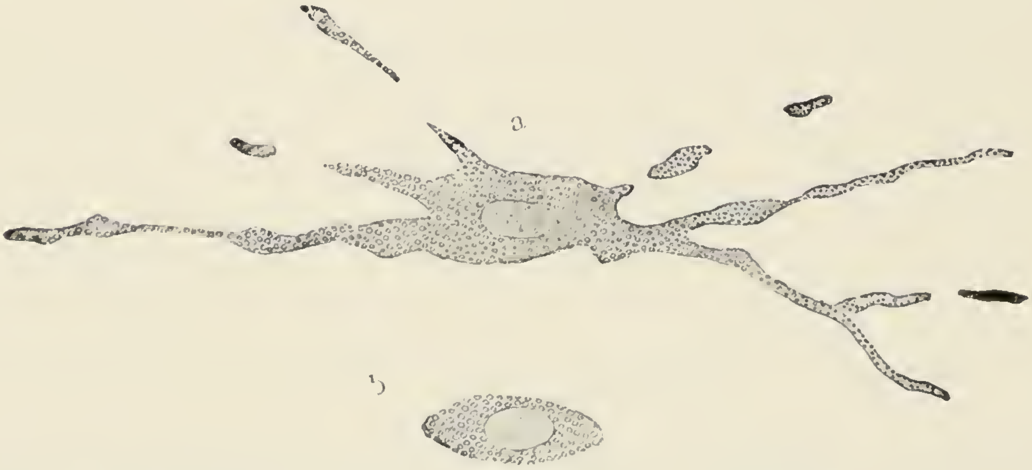


FIG. 3.—Clasmatocyte of triton after Ranvier. (a) Active. (b) Passive.

The glands—or rather, those that are visible, roughly speaking, vary in size from that of the merest pin's head to that of an almond. There is no limit to their numbers in different individuals, and they are distributed more or less unsymmetrically throughout the body.[4] They are aggregated, for excellent reasons, at certain points, chiefly under the skin *at the flexures*. They are also found in the trunk at sites corresponding to the Respiratory, Alimentary, and Uro-genital Tracts, here for certain reasons they are less in evidence. They drain various sectional regions, *only anastomosing with one another at the periphery* by their capillary vessels, between intercellular spaces. The brain and spinal cord, encased safely in their bony frame work, are more or less devoid of them.[5]

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[4] Poirier, Cuneo and Delamere. "The Lymphatics." Translated by Cecil H. Leaf, M.B., F.R.C.S. 1903.

In lower animal forms, the lymphatic system has no glands, and rising in the animal scale those that inhabit a more septic environment have more glands than those found in purer regions—such as birds.

In relation to the arterial and venous system they are paravascular, but their peripheral capillaries are epi-vascular, corresponding to the peripheral channels in the Leucocytic cell.

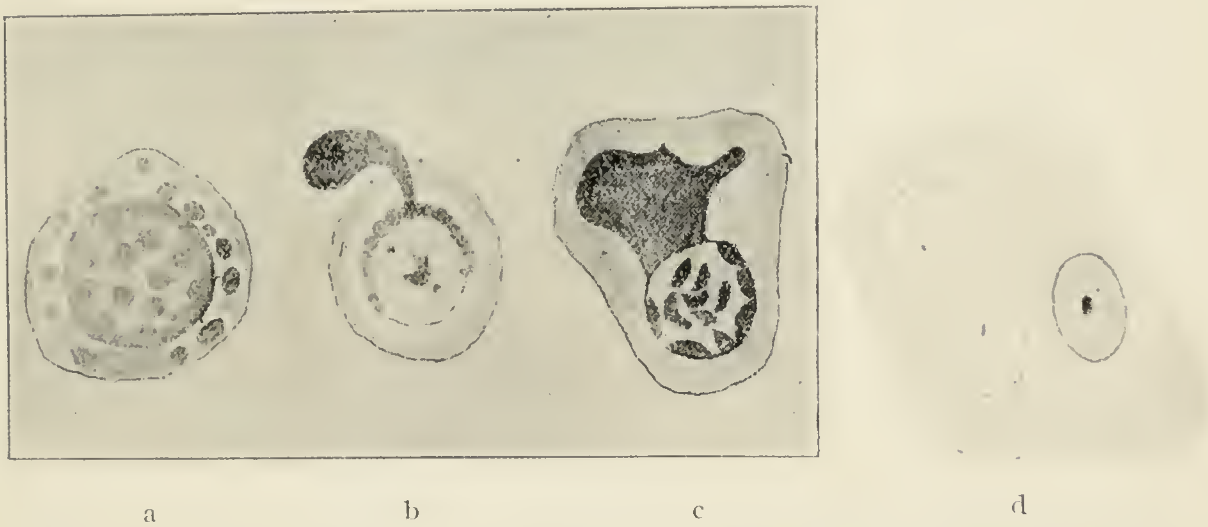

FIG. 4.—Leucocytes undergoing physiological and pathological degenerations, in which plasmosomes and filamental reticulum are involved—(a), (b) and (c) (after Adami); (d). Cancer cell (Archoplasmic vesicle), with Plimmers bodies (after Miller).

It is necessary to mention, incidentally, a peculiar property of these glands. I refer to their power of regeneration. In the case of other glands in the body, which occur symmetrically in pairs, such as the kidneys, it is well known that, when one is surgically removed, or destroyed from some cause, its fellow increases in size in order to compensate for the loss. This property is still more marked in the case of the numerous unsymmetrical lymphatic glands which seem to come into being wherever they are required for the needs of the body. This power of regenerating themselves independently is peculiar to them, and has a most important bearing in the economy. In fact, a phagocyte may be looked upon as a minute lymphatic gland on the move, for it is capable of performing the complete functions of a lymphatic gland, under certain suitable conditions.

" We must admit that our knowledge of the evolution of functions is very far from being as complete as our acquaintance with the evolution of structures. One might say in fact that the whole science of evolution has almost confined itself to the study of structures; the evolution of *functions* hardly exists even in name. Ontogeny is a recapitulation of phylogeny, that is to say, that the series of forms through which the individual organism passes during its development from the ovum to the complete bodily structure is a brief, condensed repetition of the long series of forms which the original ancestors of the said organism, or the ancestral forms of the species, have passed through from the earliest period of organic life down to the present day."[6] This occurs in response to "the Law of Environment." It should therefore be clear that the ontogeny of the leucocyte can only be understood in the light of its phylogeny (or development in the past)—both as regards function and structure. And here I would refer the reader to Professor Adami's classic article on Inflammation in Allbut's System of Medecine, Vol I.

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[5] The medulla of bone, termed " lymphoid tissue " by Von Noorden, may be closely concerned with anabolism of lymphoid glands.

To pass on to the questions quoted above I venture to suggest the following answers :—

(1). The physiological rôle of the lymphatic system has, I believe, been established as that of the sanitary or eliminatory and defensive mechanism of the body. It is the great purifier and indeed utiliser of noxæ in the tissues ; and its action is controlled by nerves corresponding to the vaso-dilator and vaso-constrictor nerves, as well as by the hormones of the extra-vascular plasma, in which it is bathed and it also has its vasæ vasorum.

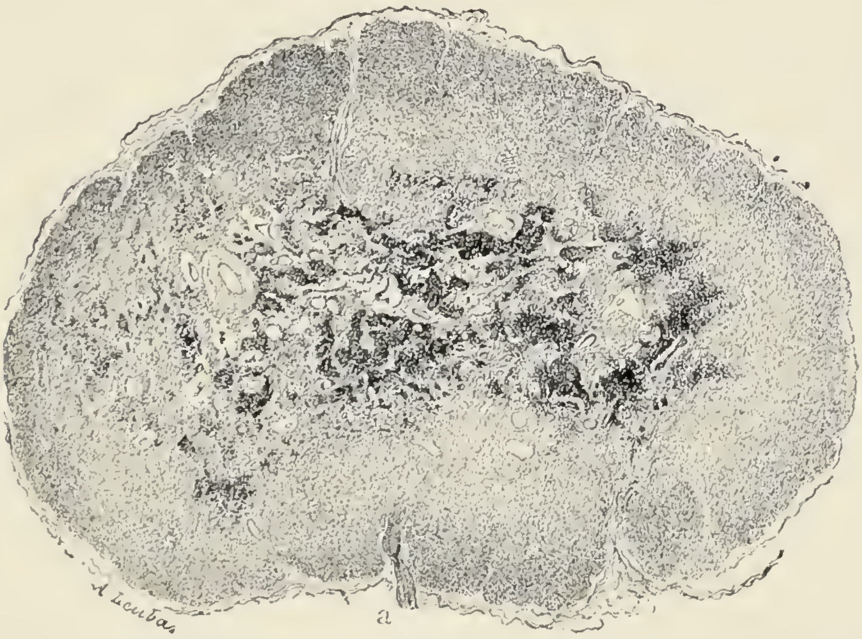

FIG. 5.—Lymphatic gland (broncho-tracheal) of the dog. Carbon particles in gland reservoir. (a) Entrance of afferent duct. Evidence of functional atrophy or immaturity of gland (after Delamere). Note radially arranged stroma elements.

"Lymph is thus extra-vascular plasma, differing from blood plasma in containing less albuminous material, and holding also the waste elements derived from the tissues, having also the nucleated, but not the non-nucleated copuscules. It would be genetically more accurate to reverse the statement of the relationship and to call blood intra-vascular lymph, in which are contained red corpuscles. Lymph may be regarded as the primary nutrient fluid, and blood as lymph plus a respiratory provision in the form of the non-nucleated corpusules, for the conveyance of oxygen to the tissues."[7]

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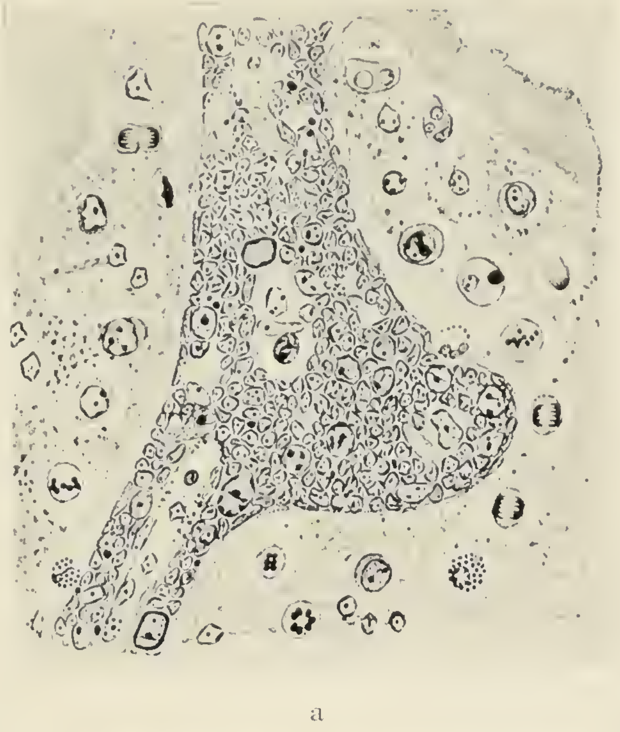
[6] Haeckel.

[7] "Human Anatomy." MacAlister.

Leucopœisis.

(2). Normally the leucoblasts are specially developed in the matrix or stroma of the lymphatic glands from their germinal layers, in response to plasmic influences and to nerve stimuli reflected to them, and these originate by the stimulation of certain peripheral sensory nerves. To meet extraordinary emergencies, as in peripheral infection by micro-organisms, one or more of the glands enlarge, and become active in the production of leucocytes which for the most part include the polynuclear and mono-nuclear leucocytes. This action is similar to the enlargement of the ovary during the period of ovulation. The lymphatic glands, being eminently cytogenous, are known to be analogous to the ovary and to the testis in this respect, but where the ovary produces, from its graafian follicle, one solitary ovum, these glands wherever required produce hundreds of leucocytes, which have the power of reproducing themselves after extrusion into the intercellular spaces in their immediate vicinity. They are extruded through the periphery of the gland, much in the same manner as the ovum from the ovary.



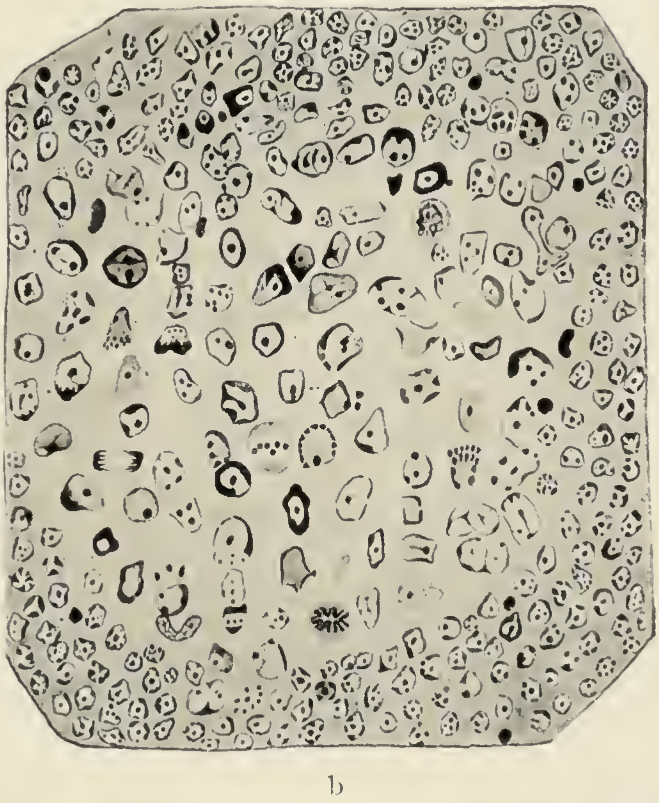


FIG. 6.—(a) Filamental medullary channel from germinal follicle of mesenteric lymphatic gland of rabbit after therapeutic intra-venous injection of pilocarpine showing leucoblastic mitosis. (b) Germinatival centre of gland follicle (mesenteric) of the guinea-pig, presenting nuclear mitosis (after Delamere).

They are gifted with powers of amœbic movement, and by the force of positive chemiotaxis are directed to the site of the infection. They

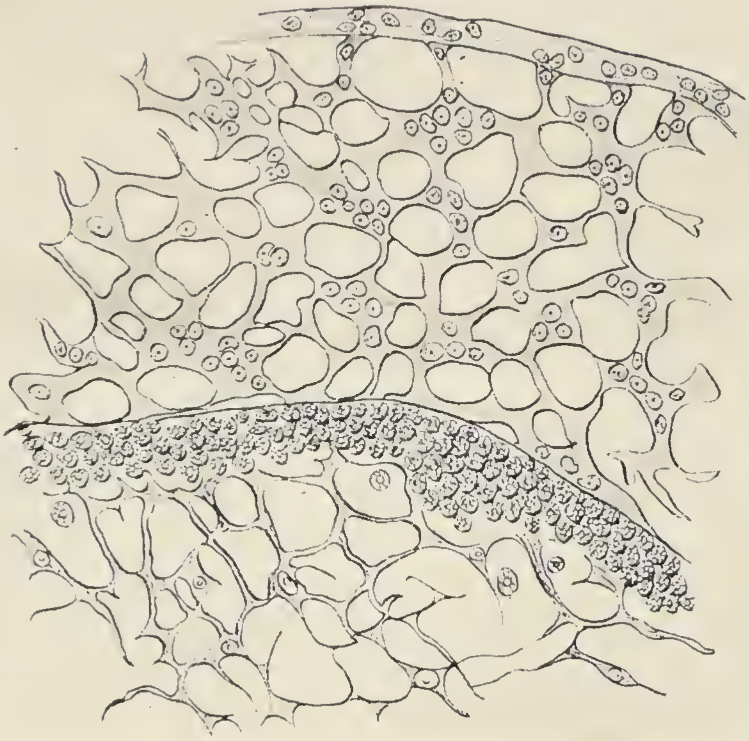


FIG. 7.—Part of section through cervical lymphatic gland of the dog, swollen to the size of a hazel-nut consequent upon inflammation of the lips artificially produced 1/500 (after Billroth). Showing centrifugal emission of leucocytes conducing to leucocytosis.

permeate the less resisting tissues, and in their passage across innumerable blood streams they are invigorated by the oxygen they pick up; numbers are swept away in the currents of blood, and from these they emerge at other points, whence they continue to move in the required directions. They are the denizens of the plasma, and their presence in the blood stream is more accidental than natural.

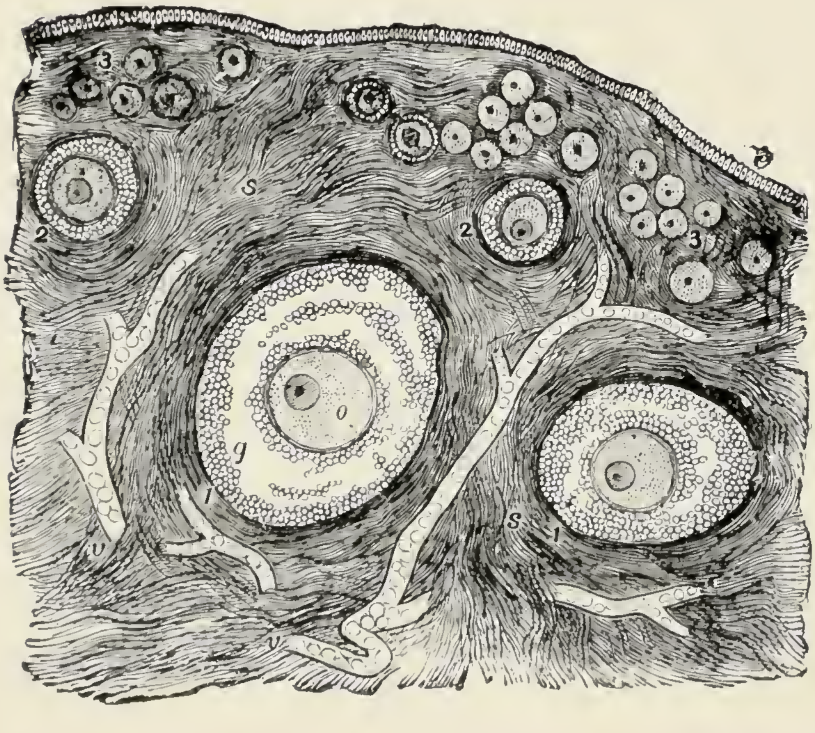


FIG. 8.—Section of human ovary, showing radial arrangement of stroma elements, embedded in which are the graafian follicles, the largest of which are internal and they grow towards the surface. 1/30 (after MacAlister).

Phagocytosis and its sequelæ.

(3). These cells perform phagocytosis of the opsonized micro-organisms, under certain conditions; and, where these conditions fail, others perform "segregation." Where complete phagocytosis is alone required, and physiologically effected, the satiated phagocytes *make their way back to the lymphatic glands concerned, by way of the nearest lymphatic ducts,* which circumjacently abound, conveying particles of organic and inorganic matter to those glands, which are their

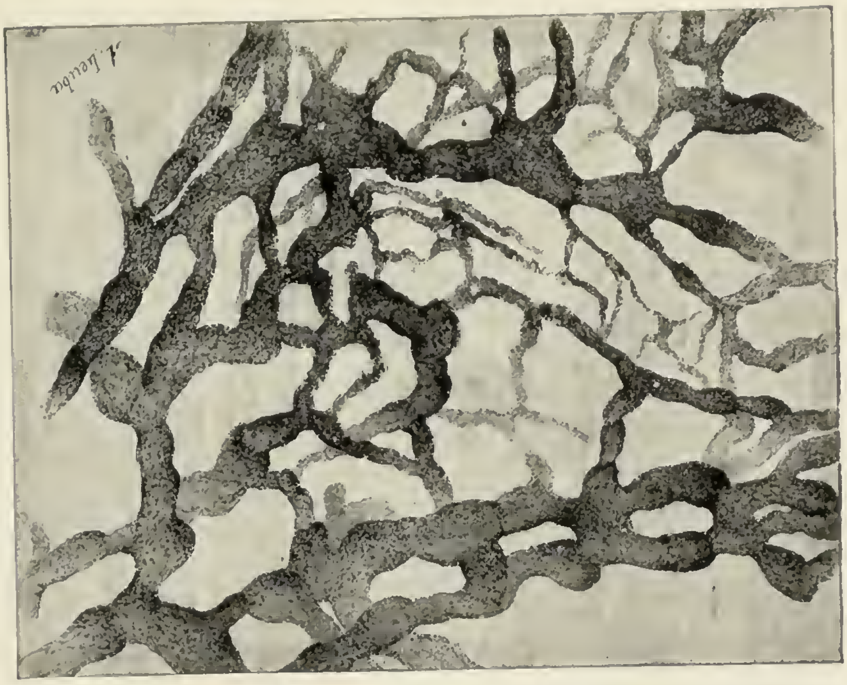


FIG. 9.—Lymphatic network of the subserous gastric layer of the rabbit, the fainter and deeper valveless layer being the sub-serous plexus. Note convergence in one direction, namely, lower left-hand corner of figure (after Delamere).

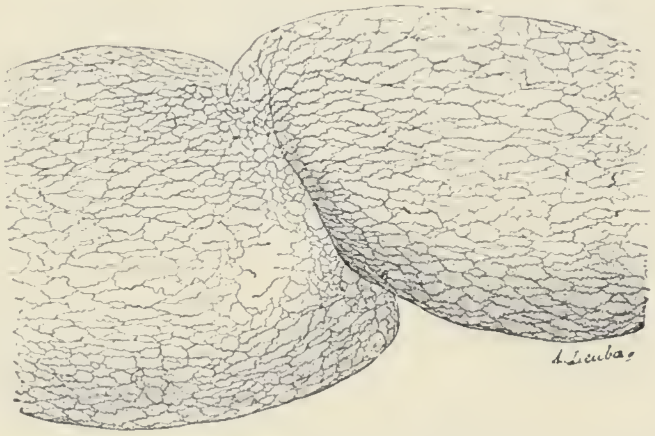
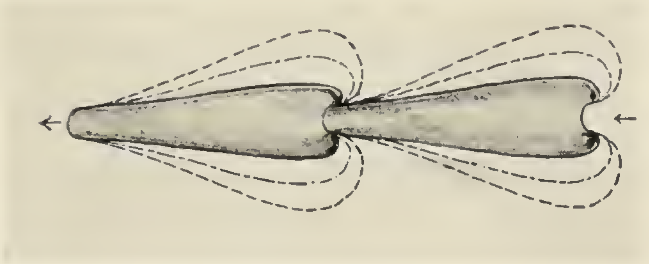


FIG. 10.—(a) Valve of gastric subserous human lymphatic radicle, viewed externally, removed by operation, showing "cleft" or "crevice" (after Delamere).



(b) Diagram of bi-section of lymphatic radicle at valve, illustrating function—the rim of valvular ring should be shown internally, in apposition at full expansion. [8]

respective destinations and they affect an entrance by way of the afferent ducts. They do so notwithstanding that their amœbic mobility is, at this stage, considerably lessened, and that this phase of chemiotaxis is now on the wane. They arrive at the wedge-shaped "clefts" or "crevices," which lie very closely together in the course of these ducts, by the force of negative chemiotaxis, and they insinuate themselves between the inclining sides of these "clefts," till they gain entrance into the ducts. They then glide into the dilated expansions, known as the "valves," whence, after temporary accommodation, clasmatosis, which is a physiological degeneration, takes place, and their remains are propelled to the gland reservoir, where a chemical dissociation and re-arrangement of their constituents is brought about. This is completed by the time their remains arrive in the reservoir of the gland, where it is conceivable that a final change of their chemical

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[8] The action of adrenalin injected intra-peritoneally, as demonstrated by Sir James Barr in peritoneal effusions, would suggest its tonic action on all the lymphatic ducts, and this may be its physiological function in the economy.

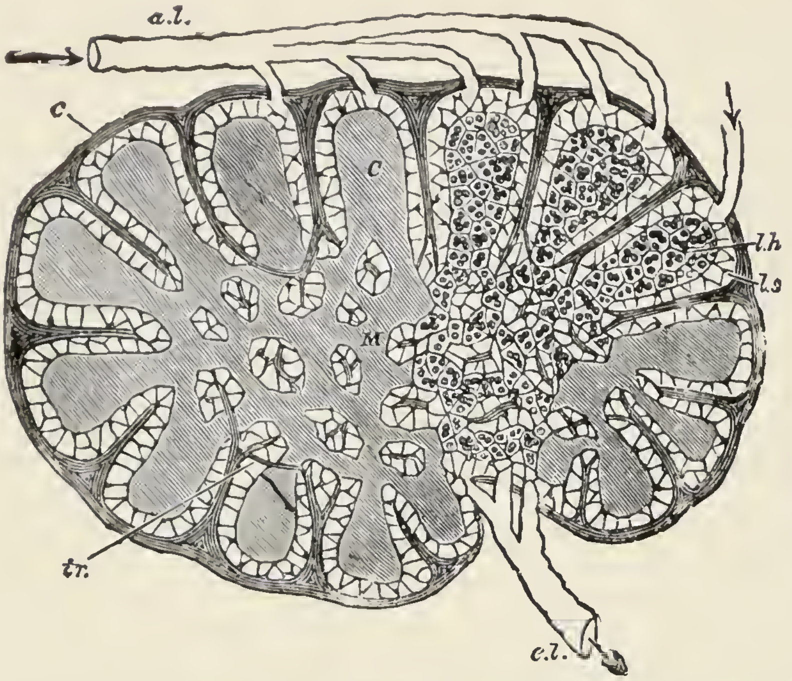


FIG. 11.—Schema of lymphatic gland, showing afferent and efferent ducts. Here the true afferent duct is shown as the efferent duct, e. l. being the afferent duct. (after MacAlister).

constituents into an immunizing agent occurs; and it is the purpose of this paper to put forward the thesis that such a change does actually take place in the gland, as under simpler conditions, actually takes place in the phagocyte itself. This substance is a self-elaborated bacterio-tropic and anti-toxic vaccine. With it the plasm or plasma first, and the blood afterwards, is sensitized, thereby conferring upon the individual concerned,

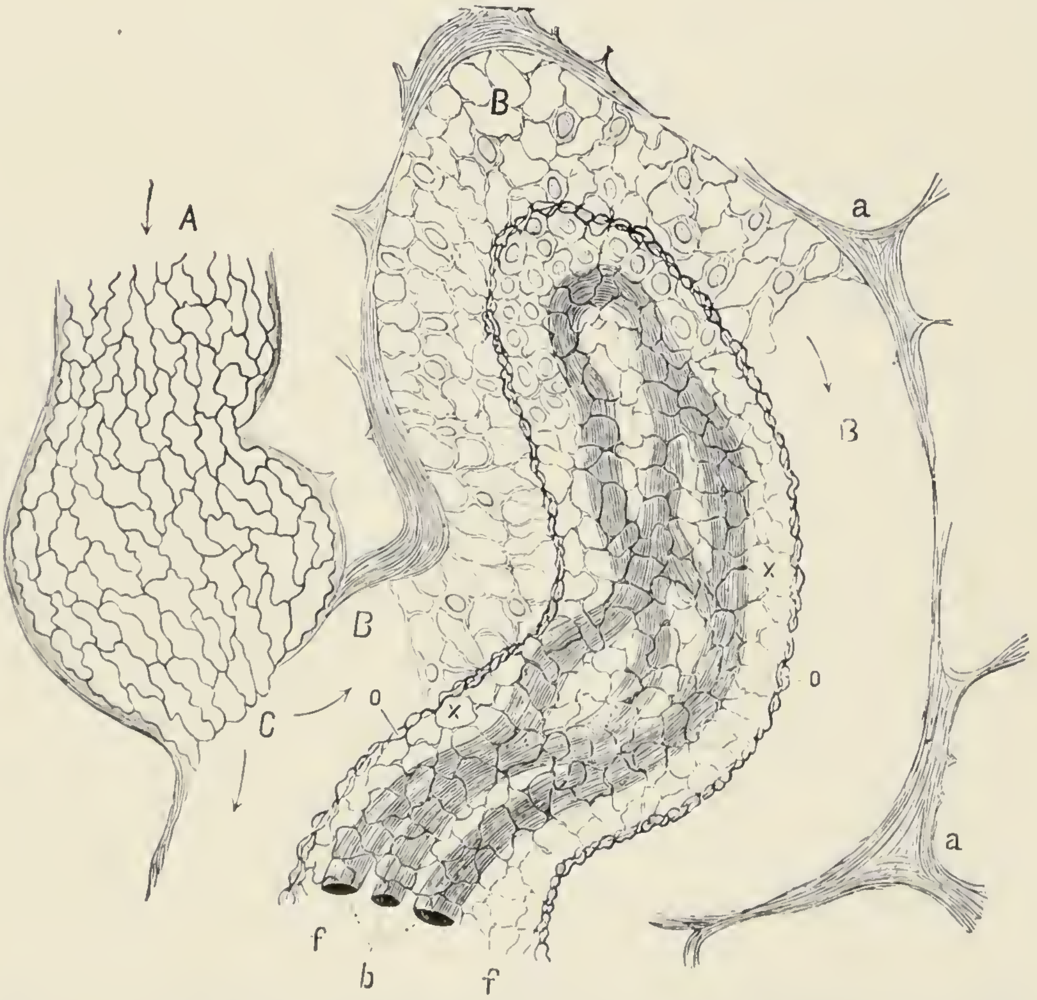
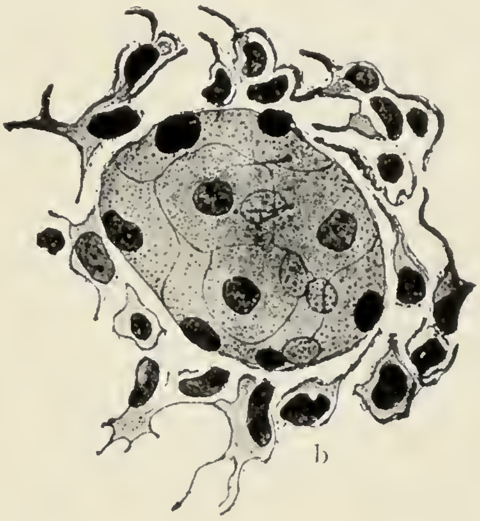


FIG. 12.—Diagram of lymphatic gland. (A) Vas afferens, (B) lymph space or "gland reservoir." (a) Lymph spaces external to gland periphery which give rise to the idea of afferent ducts as in Fig. 11. (f) Process of medullary mass germinatival centre surrounded by gland follicles x; (O) condensed layer separating adenoid tissue from stroma of filamental reticulum or trabeculæ and (b) blood vessels. (after MacAlister).

varying degrees of immunity against that particular infection. But it is very doubtful whether this is effected by way of the efferent ducts, whose existence, the present writer would even go so far as to question. It seems more likely to be, by an osmotic transudation through the hilar membrane, in the concavity of the gland and on the floor of the reservoir, thus passing into the intercellular space external to it—more particularly during the process of shrinkage, which takes place on the approaching cessation of glandular activity. No reverse flow by the afferent ducts would appear to be possible under any circumstances during their active state, when the remarkable valvular structure of these ducts is considered. Moreover the anatomical representations of efferent ducts originating from a lymphatic gland in text books of human anatomy have been admittedly schematic, and their actual existence. has not so far been demonstrated with any satisfaction. The schema is unconvincing, and morphologically inconsistent—the gland, in the writer's opinion, being a medusa-like body. It should be borne in mind that this gland is not so much a secretory, as it is a gametogenetic gland of the first order. and in this respect it excels the spleen.[9] to which it is functionally related in its production of non-nucleated red cells. The actual representation of a lymphatic gland on the other hand, is invariably shown with its afferent ducts entering at the hilum and at no other part; the vasæ efferentiæ so called, are merely intercellular lymph paths and not vessels in the sense of tubes or ducts.



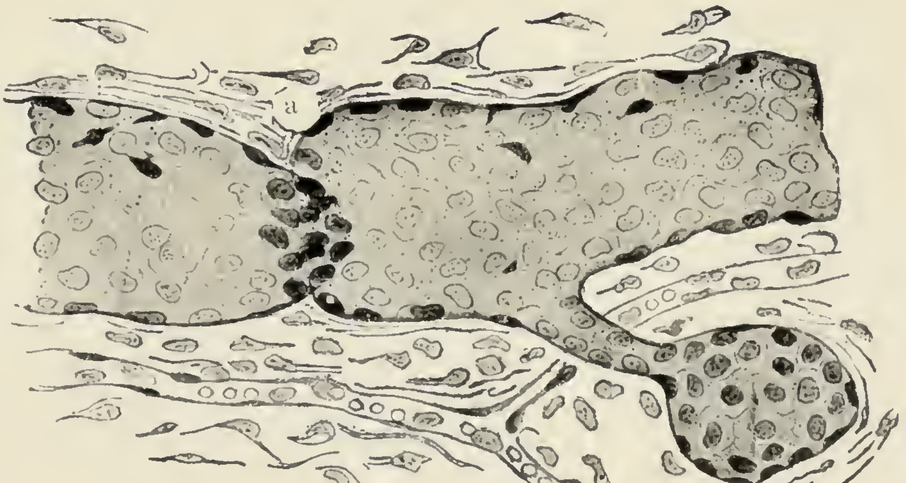


Fig. 13a.—Lymphatics in involution: lymphatic vesicle in continuity with lymphatic radicle, showing (a) "cleft" or "crevice" at valve with leucocytes in the act of gaining entrance into the duct from without; the valve orifice being occupied by physiologically (?) degenerated leucocytes, in their progress to the gland chamber. (b) Isolated vesicle (after Ranvier).

If we refer to the anatomical demonstrations of the lymphatics of the

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[9] The filamental germinal channels in the Malpighian bodies of the spleen open *directly* into the *venous capillaries of origin* which drain these bodies.

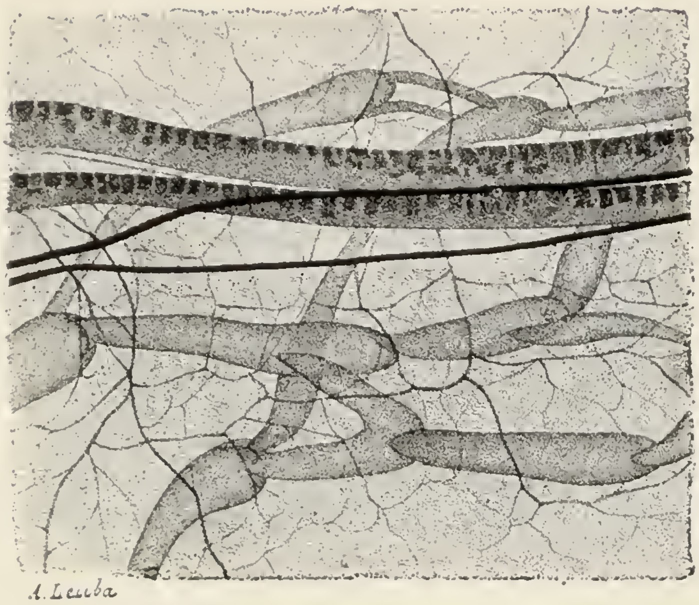

FIG. 13.—(b) Valves of the mesenteric chyliferous radicles of the new born cat. Note absence of anastomosis in its true sense, of valved ducts, all being directed afferently (after Delamere).

abdominal organs on the one hand, and those of the skin of the chest wall, for example, on the other. (I refer to Gerotas method of injection). In the former case we find that the duct radicles originate in the valveless sub-mucous and subserous lymphatic capillaries, and they converge by valved roots to a point, whence they are continued in one single stem-duct to the nearest lymphatic gland. In this one or more such duct-stems terminate all *being afferent ducts.* Such a stem-duct may pass one gland, seeming to communicate with it, on to the next internal to it. I am not aware of the *direct* intercommunication of one lymphatic gland with another, nor of the ducts of one gland communicating with the ducts of another. This feature is very clearly shown in the demonstrations referred to above.[10] But there is no doubt that the sub-mucous and subserous capillary lymphatic plexuses, being valveless, communicate with one another, as well as with the sub-epidermic and sub-cuticular plexuses by anastomosis, where skin and mucous membrane meet one another. Fig. 14B.

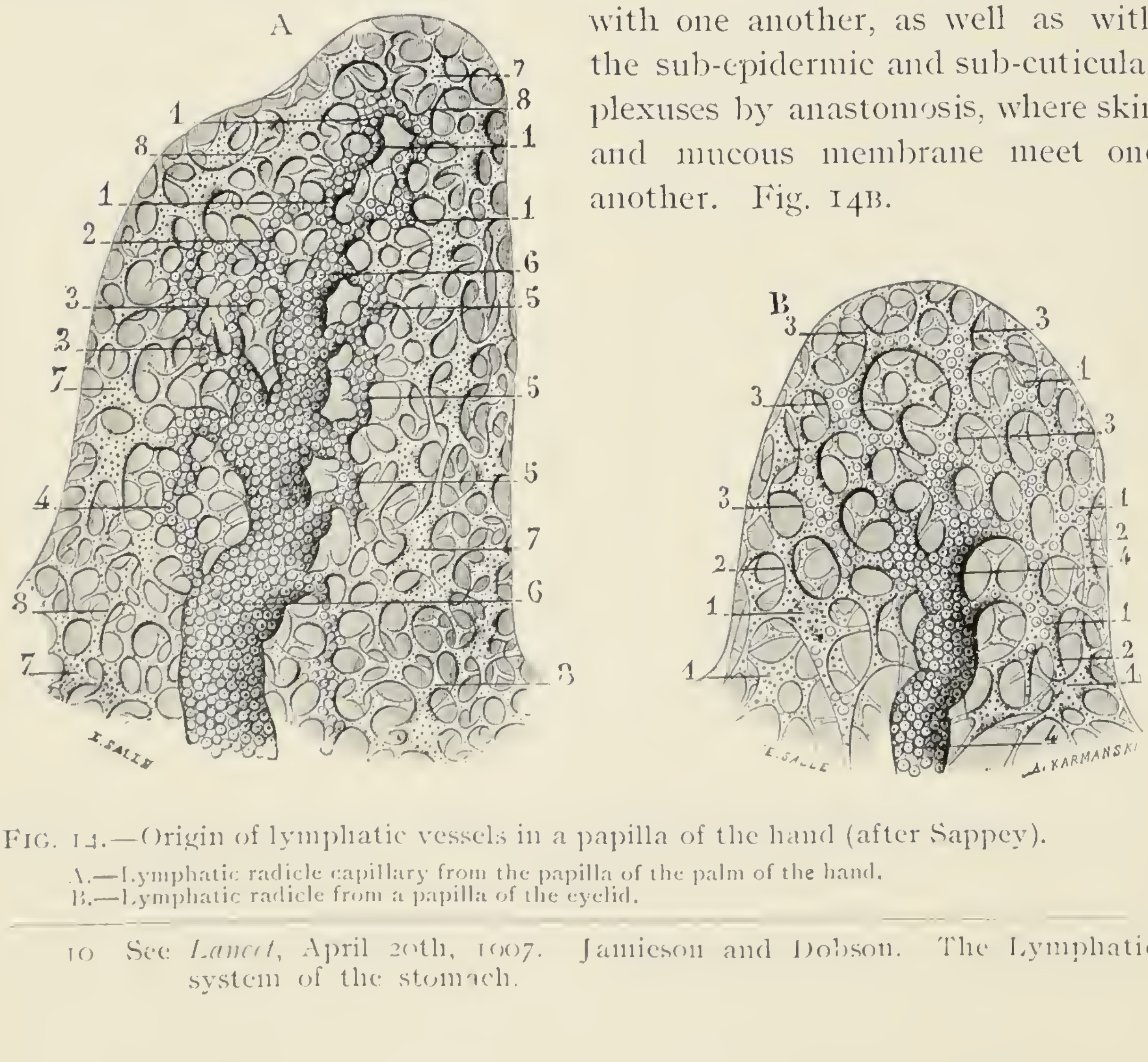

FIG. 14.—Origin of lymphatic vessels in a papilla of the hand (after Sappey).

A.—Lymphatic radicle capillary from the papilla of the palm of the hand.
B.—Lymphatic radicle from a papilla of the eyelid.

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[10] See *Lancet*, April 20th, 1907. Jamieson and Dobson. The Lymphatic system of the stomach.

It should be borne in mind that, as these lymphatic capillaries[11] originate from cæcal ends, they have no direct connection with the lymphoid or solitary glands on the one hand or the "large prickle cells" on the other. In the chest wall or skin the lymphatic duct radicles originate in a similar fashion to form stem-ducts, which proceed, some to the outer, and others to the inner zones of lymphatic glands. The anatomical disposition of the lymphatic system is therefore in three concentric circles. (Fig. 22.)

The outermost of these circles represents the sub-mucous lymphoid follicles and large prickle cells, the narrow circular band represents the originating lymphatic capillaries, namely, the two layers which are sub-mucous and subserous on the one hand and sub-epidermic and sub-cuticular on the other.

The inner circle represents the outer zone of lymphatic glands whose duct radicles usually accompany the veins and arterioles. The apices of the star-like figure indicate the inner zone of lymphatic glands, while the innermost circle represents the most internal glands. This is the central zone of lymyhatic glands and includes the thoracic duct. The interspaces represent the serous cavities and intercellular spaces of the body. In regard to the disposition and relation of the lymphatic system and the central arterial system we have in the tortoise a remarkable analogy where the lumen of an artery on transverse section is shown to be within the lumen of its lymphatic vessel which though valveless is fistulated. (See MacAlister's Human Anatomy). The vitality of the tortoise is the greatest known at the present time.

The large prickle cells, so like the "so called" fixed connective tissue cells, lend themselves as future lymphoid gland matrices, in order to meet special emergencies. This occurs in response to peculiar cutaneous stimuli such for example as those of the toxin of vaccinia, on its insertion after scarification of the epidermis. So that in the case of a vaccine vesicle, or for the matter of that, any skin infected vesicle, rudimentary lymphoid tissue is formed around the point, causing that part of the cutis to stand out in relief in consequence of the local leucocytosis. This tissue fulfils the function of a lymphoid gland and degeneration and resolution follow, but not without causing a temporary breach or defect in the line of lymphatic defence at such a point—hence the danger of other extraneous toxic and microbic invasions at such—to wit staphylococcic stroptococcic or erisepelatous (Fig. 15).

To pass on to the consideration of the functional development of the solitary gland ; we have under the epithelial layer the cone or sphere-like summit covered by a basement membrane. Under this, on either side of the cone, is a fine stroma, containing the germinal follicles encircling the cone, which is composed of medullary substance like the malpighian body in the spleen. Within this medullary substance filamental channels are seen, which converge to its base, forming branched V or Y like figures. These channels indicate the direction in which the leucoblasts, which are formed in the germinal layer of the medullary substance, travel. These cells are generated in response to the stimuli of metabolism or chemiotaxis. During this process, the cone of the gland, as it were, recedes at

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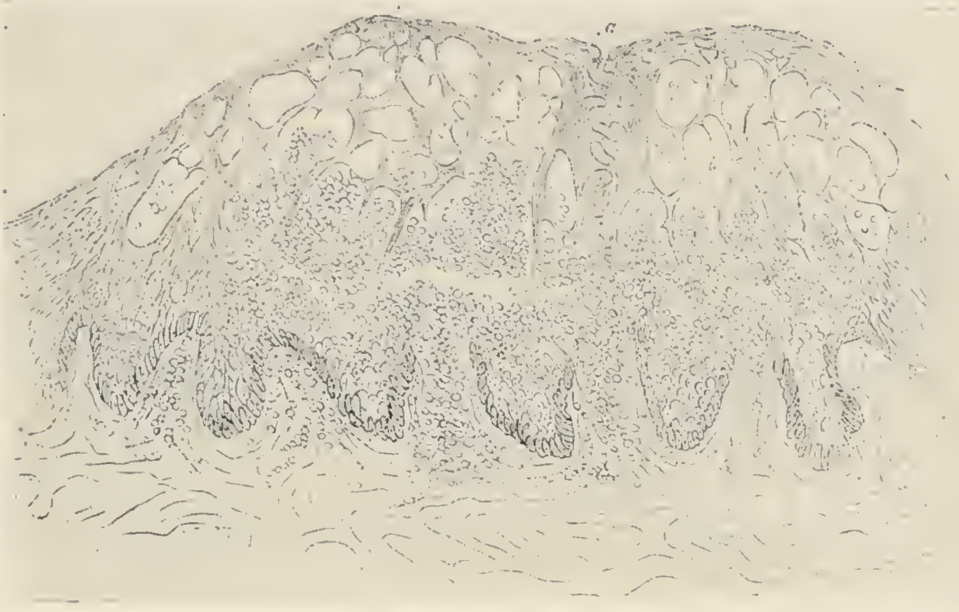
[11] This term capillaries is confusing, when speaking of this system on account of its meaning in regard to the arterial and venous systems. It is only apt in relation to the venous radicles of the Malpighian bodies of the spleen.



the expense of the medullary substance, and a dimple or umbilication appears on the surface of the mucous membrane. This gives rise to the formation of a chamber at its summit, which corresponds to the lymphatic gland reservoir. Into this chamber the leucocytes enter, having performed their function, and their physiological degeneration or clasmatosis is brought about by katalytic action.

FIG. 15.—Vertical section through the middle of a pock passing from the papular to the pustular stage. (a) "Umbilicus" with duct of sweat gland; (b) Loculi formed by separation of the lamellæ and filled with lymph (after Rindfleisch 1/500). These are the spaces previously occupied by the "large prickle cells" which in the mechanism of defence, acting as lymphoid matrices, became transformed into lymphoid tissue, in which the physiological degeneration or clasmatosis of the leucocytes took place, resulting in the lymphoid tissue destruction and the formation of the vaccine or enzyme which is known to be both anti-toxic and anti-microbic, after the fourth and until the fifth day of "maturation."

The resulting secretion containing its enzymes, transudes on to the mucous surface, and thus influences the different fermentations in progress there. Fig. 20 a and b.

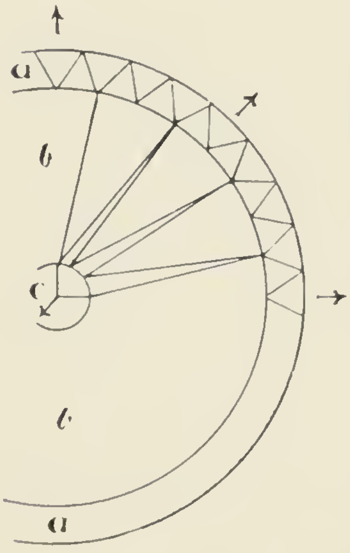


FIG. 16.—Diagram illustrating the lines of lymphatic defence from the cutaneous surface inwards. a The two layers of origin of lymphatic plexuses. b The zone of the three lines of lymphatic glands. c The arterial and venous systems.

I might mention incidentally in the above reference, that in the Lexicon of Medicine and allied Sciences (New Sydenham Soc.), the definition of Metastasis in a physiological sense, is given as follows :—"The process of chemical change whereby a living tissue converts new dead matter into another form of dead matter, in contra-distinction to metabolism." This would correspond to the 'clasmatosis' of Ranvier.

"The time honoured comparison of the lymphatic gland to a filter is only partly accurate or apposite, because it leaves out of count the most important of the functions of the gland, namely, the vital action of the cells which inhabit it. In all probability in health this action is largely a chemical one.[12] It is a well-known fact that in many of these bacterial infections, at the height of the lymphatic glandular activity, *bacteria, as well as leococytes*, are conspicuous by their absence from the gland reservoir. The contents of which have been found to be sterile. In the British Medical Journal, January 27th, 1906, will be found these words: "The axillary lymphatic glands were sent for examination. Mr. Ernest Shaw, whose histological skill is acknowledged, reported that the *large glands*[13] did not contain cancer, but that some minute ones did. This too, Mr. Shaw tells me, is an *ordinary* experience." This is also confirmed by Dr. Mallanah, in the "Lancet" of January 26th last, in regard to the infection of Bacillus pestis in rats, the glandular extract of which he used successfully as a curative agent in plague inocculated rats; also by Dr. Peter Paterson, re tuberculosis.,[14] and by Dr. P. G. Wooley, see note on p. 33.

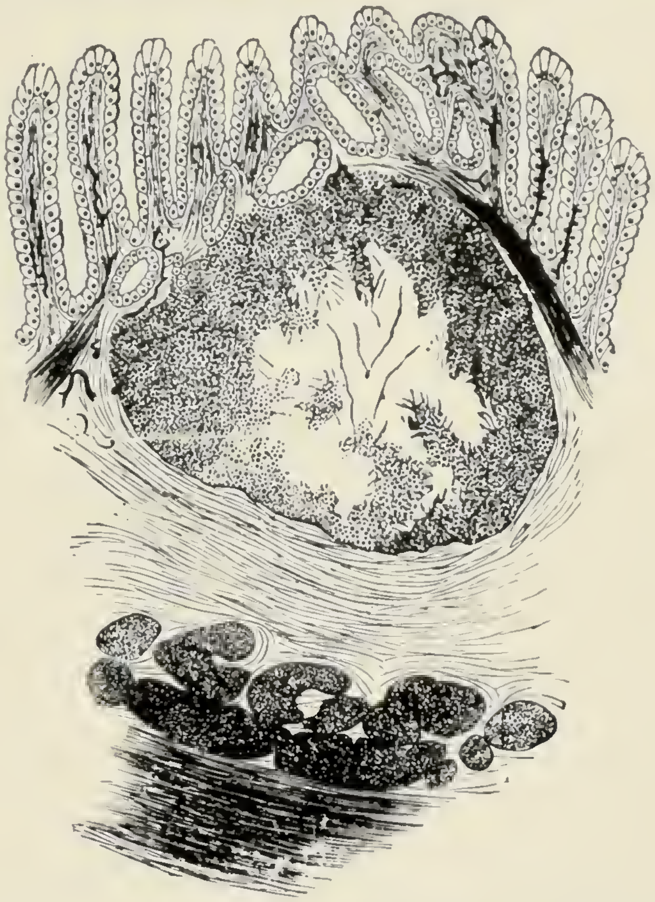


Fig. 17.—Solitary or lymphoid follicle, mature and at rest. Note germinal follicles above medullary sub stance or malpighian body and under basement epithelial layer, also Y-shaped filamental medullary channels converging downwards to basal periphery of gland (after Macalister). The separation of the lamellæ in formation of clasmatic chamber or reservoir only appears on functional activity of the gland, and is therefore not visible above follicles and cone. See Fig. 18.

"If the contents of the smallpock be collected with antiseptic precautions, it will almost invariably be found sterile up to the seventh or eighth day of the eruption. On this day, pyogenic organisms, such as the three well-known varieties of staphylococci (which abound in the skin surface), appear in the vesicular contents."[15] It is well known that the secondary fever of smallpox is the sequela of the coincidental invasion of the vesicular chamber of the pock by these micro-organisms.

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[12] Encyclo. Medica.

[13] The italics are mine.

[14] The Lancet. 25th Aug., 1906. 23rd Feb., 1907.

[15] The British Medical Journal, Vol. II, 1906, p. 1576. Dr. W. E. de Korte.

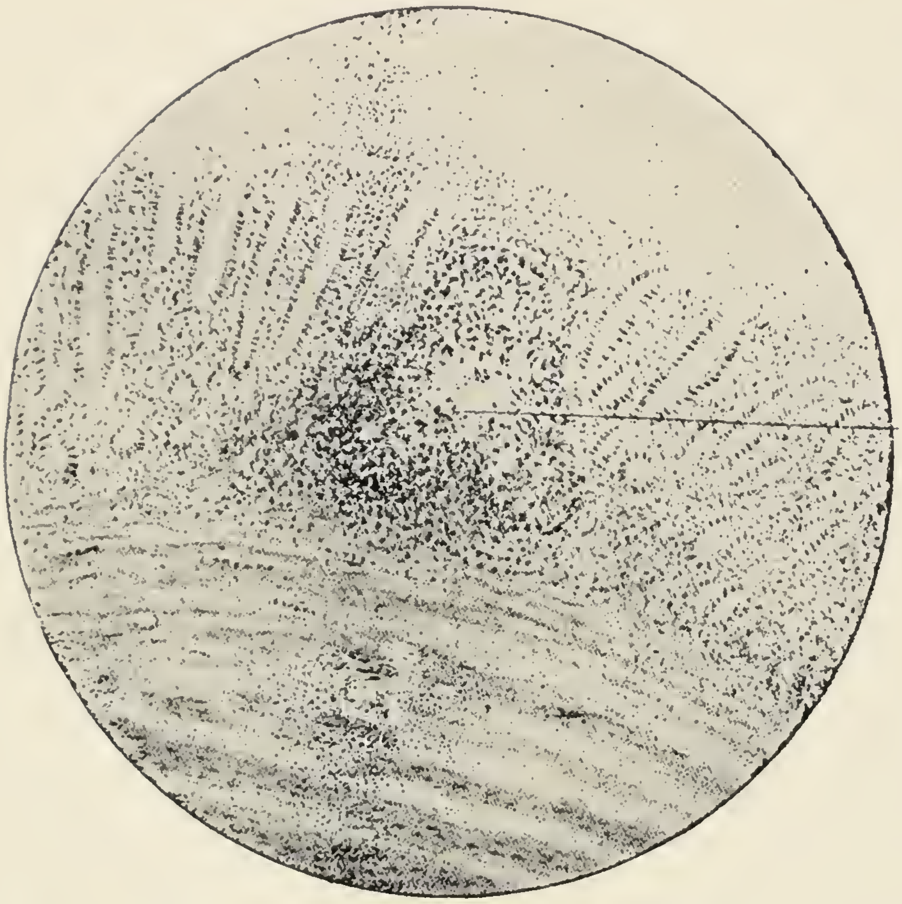

Fig. 18.—Solitary or Lymphoid follicle in function from human stomach. Note recession and degeneration of germinal follicles into medullary substance. The delicate pelicle on the cone of the gland has been destroyed along with its epithelial covering, and the secretion resulting from the chemiotactic process has passed out on to the mucous surface. (after Miller).

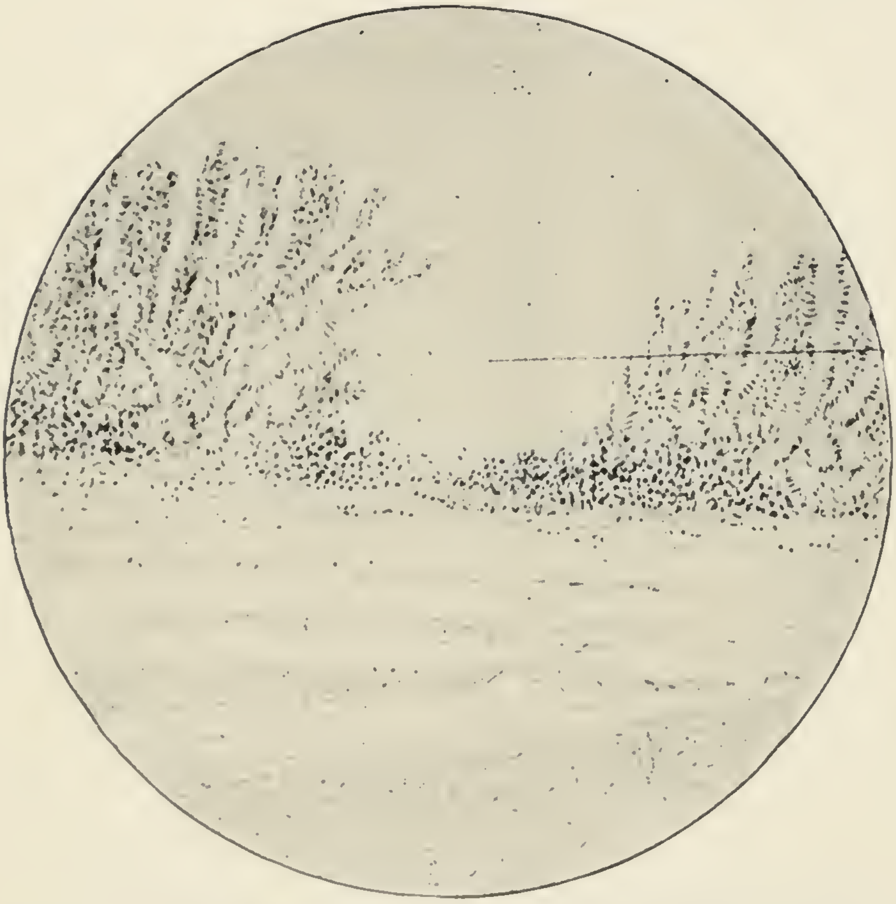

Fig. 19.—a The space of the degenerated lymphoid follicle. (after Miller).

I have tried to show that the appearance of the vesicle is in consequence of the formation of rudimentary lymphoid tissue, in which the large prickle cells underlying the epidermis play the part of lymphatic matrices, in order to facilitate this formation, under certain circumstances. This takes place in the chemiotactic process of bodily defence. I also hope to show why it is that the floor of this vesicular chamber exposes the body to reinfection by toxic micro-organisms. It is also known that these same micro-organisms invade the chamber of any skin blister artificially produced, for example, in the blister resulting from a little hot sealing-wax falling on the finger. I have made cultures of all three varieties of staphlococci from such a blister, with aseptic precautions. In such blisters, as well as in the vesicles of *lichen tropicus*, I have found them to be non-pyogenic, if the lymphatic reticulum below escapes injury, a fact that can easily be proved experimentally.

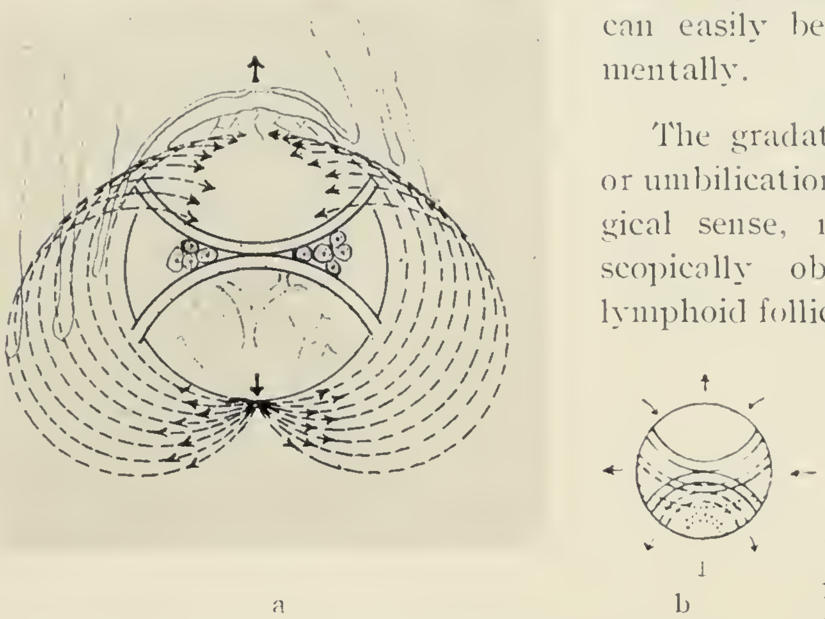

FIG. 20.—(a) Diagram illustrating chemiotactic and katabolic action in a lymphoid follicle. (b) Diagram illustrating pro-cession of the solitary gland in the process of involution and its re-cession in the process of physiological degeneration.

The gradations of dimpling or umbilication, in a physiological sense, may be macroscopically observed in the lymphoid follicles of the tongue, and the tonsils, as well as in Peyers patches.

On the occurrence of peculiar micro-organic or inorganic stimuli to the muco-cutaneous body periphery, in its special environment, action would be set up in the following order.

[*] The plasmic hormones and the peripheral sensory nerves, followed by nerve reflex, solitary gland or "large prickle cell" or lymphatic gland, and Leucopoeisis, Leucytosis, Phagocytosis, Clasmatosis, Sensitisation of the body plasma, and lastly Immunity.

These processes being those of exalted metabolism, the normal metabolic process would be disturbed. The lymphoid glands are pre-eminently concerned with the elimination of innumerable exogenetic toxins, as well as with local histogenetic functions. Their peculiar anatomical position is suggestive of these methods of function, as is also the fact of their destruction, in the achievement of immunity. Fig. 19.

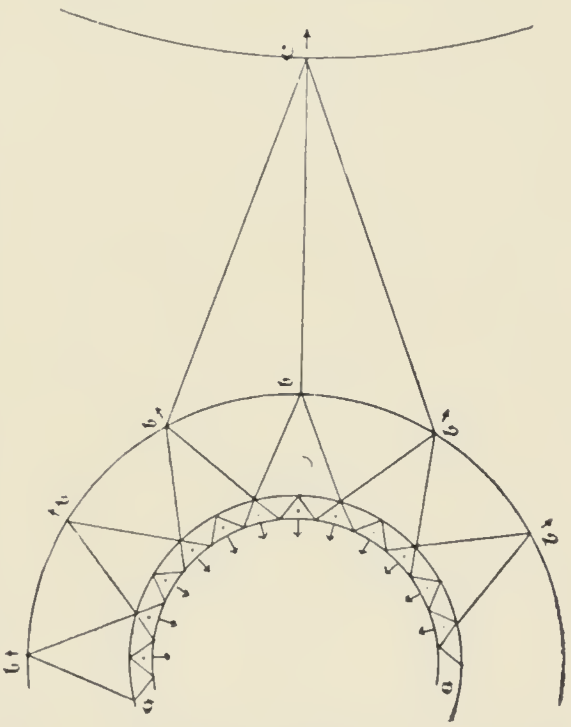

FIG. 21.—Diagram of intestinal or mucous lymphatic defence inwards, a to c includes the three lines of lymphatic defence.

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[*] The plasmic hormones and their action were first described by Professor Starling, of University College, London.

What becomes of the surfeited phagocytis?

(4). Where there is a defect in regard to the co-ordination of the processes of "opsonization," "incitation," and the due supply of phagocytes, then the phagocytes present become oversatiated; they are in an abnormal state and therefore do not go far on their return journey by the force of negative chemiotaxis alone. They have, in fact, become moribund. This occurrence marks the inception of the pathological stage. The moribund phagocytes are then surrounded by the segregating leucocytes, and disruption of their cytoplasm may thereby be averted. These are unscientifically termed "giant cells," and one or more of these cells may in this manner be enveloped by the segregating leucocytes. The cytolytic action of the cancer *coccus* on the phagocyte tending to its amyloid degeneration should be borne in mind. At times these segregating leucocytes will go on piling up tissue cells, producing a veritable stroma; and, in doing so, will be influenced by the destruction of the local normal cell structure. This results in a crude replica of the tissue being produced, even to the extent of the new tissue cells secreting bile, as illustrated in the two cases of 'primary' carcinoma of the liver of Messrs. Miller and Cleland.[16] Thus many histological varieties of cells in a stroma result. Hence we have such terms as "epithelioma," "endothelioma," "enchondroma," "osteoma," "papilloma," "cylindroma," *et hoc genus omne.* When this growth is found to occur 'primarily' (?) in the liver, as in the cases reported by Messrs. Miller and Cleland, it is difficult to give such carcinomatous tumours a name by which they can be classified. Indeed we seem to be on the transition line.[17] The initial hyperæmia of the gland in question conduces to its functional activity; but, as in the case of the ovary, it has a limited, though probably slightly longer, period of activity. In the ovary a minute scar is known to result at the point of

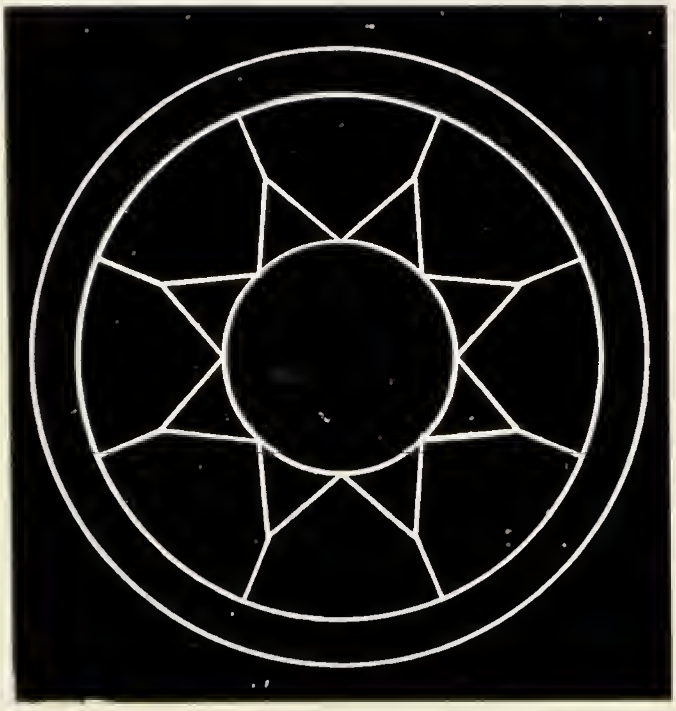

FIG. 22.—Diagram representing concentric arrangement of the lines of lymphatic defence. The central circle corresponding to the innermost line of defence. This figure is composed of the Figs. 16 and 21, the central circular space representing arterial system, including the thoracic duct.

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[16] Archiv. Pathol Instit. Lond. Hosptl. Vol. 1, 1906.

[17] Ibid.

extrusion of the ovum—so also it is conceivable that a minute repair may be necessary over the periphery of the lymphatic gland at each point from which the leucocytes have been discharged. In any case, the result is a tough fibrous capsule, coating the gland, which capsule in course of time impedes its functional powers.

Further, the gland in question may be overtaxed and its functional powers may wane and eventually cease: this marks the inception of the morbid condition of the gland in the later processes of defence. To meet this condition, the phenomenon of segregation is evoked in the same manner as described above; a veritable "Port Arthur" results, and a state of panic in the sanitary department—"the blue water school" of Dr. Dawson Williams. An earthquake, so to speak, takes place, as evidenced by a rigor and a high temperature, followed by a sweat, and the physician "sees" pus, somewhere, the condition being termed—HECTIC.

These remarks may be considered to be dramatic; but *we* know them to be tragic: so also say the leucocytes. Suppuration of the gland ensues with pus known to be sterile (once termed "laudable"); and if the integrity of the encapsulating tissues be effective then the liquid portion transudes and is absorbed. The result is caseation, which is followed by calcification, the mass being retained as a "foreign body" till otherwise disturbed; but the originally elaborated chemical vaccine of defence remains within it for lengthened periods undecomposed—like the radium in pitchblende.[18]

I venture further to maintain, from what has been stated above that the phenomenon of Metastasis in infectious diseases can be explained as a consequence of the arrest of the morbid leucocytes; these, on their return excursion, are carried to certain points about the lymphatic ducts, remote from the originally infected site, by the influence of aberrant negative chemiotaxis; and this result is prior to their envelopment. Metastasis then is effected *not by the so-called lymphatic circulation, as is generally believed. There is no true circulation in the lymphatic system.* Its outlet by the thoracic duct into the vena cava is analogous to that of the common bile duct, or to that of the pancreas into the jejunum. The movement of the fluid in the lymphatic channels is comparatively slow and intermittent. It takes place in varying directions, according to the activities of the various distal glands, except, perhaps, in the proximity of the main thoracic duct and its chief confluents, where they are brought into connection with the portal system and lacteals. The liver acts as the great incinerator and filter of debris.

When metastasis occurs in the lymphatic structures of the liver; secondary to cancer of the rectum, for example, evidences of the rectal epithelium are found in the parts of the liver *that become first* thus affected.

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[18] The greater the age of the individual, the greater is his plasmic immunity, according to his phylogenesis and the environmental influences he has passed through.

In considering the more advanced stages of a cancerous process, it should be borne in mind that the process involved in meeting the devastating action on the fixed tissues at the site of the lesion, is a double process. This is composed of the reparative process to meet tissue destruction, as well as the process of opposing the microbic invasion, the two acting concurrently. The former of these two processes predominates greatly over the latter, for reasons that may suggest themselves, viz., devastation of normal tissue by cytolysis of its cells, absence of toxins or toxin generation by the microbes which are known to be peculiarly non-toxic or non-toxin generating. A metastasis under these circumstances from the rectum to the liver, would, at the outset, result in the cells destined for the tissue repair of the rectum, being diverted to the liver by the altered chemiotaxis to the seat of such metsatasis, and this would continue until such time as the liver tissue began to be destroyed, thus evoking a response for its special repair. The special tissue repair would be effected later, depending to some extent upon the complexity of the cells of the structure requiring repair and replacement. This diversion of chemiotaxis does not take place in the other infectious secondary metastases, as the conditions are reversed, namely, the microbes are highly toxic and far less destructive to the more complex fixed tissues, permitting of easy segregation, without cytolytic effects on the cells of either the fixed or the new formed segregating tissues.

It follows, from what has been stated, that Metastasis is consequent upon imperfect segregation, and upon the failure to transfer the infection-laden phagocytes to the interior of the lymphatic afferent ducts.

In fact, the micro-organisms are found in various stages of animation in the vicinity of these ducts, *but external to them* ; and this effect is likely to be noticed so long as these ducts are intact, and not strangled by adjacent segregating tissues or blocked within. Moreover, when micro-organisms get adrift by disruption of these leucocytes in such localities, the stimuli necessary to again evoke a phagocytosis are not forthcoming. In these intercellular depths there are none of the appropriate peripheral sensory nerve terminals, and the micro-organisms find themselves " saved at last," inside " the hollow square," where the response to their stimuli is of a different and more inco-ordinate kind and dependent on the hormones. In the absence of definite phagocytosis the mechanism of defence is thus reduced to a half measure ; and a formation of masses of stroma, constituting a new growth, takes place.[19]

I have used the term " hollow square," a militant one, in regard to bodily defence, and I might have added " bayonets fixed " for a better appreciation of the simile. These we have in the "large prickle cells" which form the visible outworks of the lymphatic system at the sub-epithelial periphery of the skin and in the solitary and lymphoid follicles under the mucous membranes.

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[19] In the stomach, pylorus, colon, and bladder, the growth of cancer, is notoriously slow. The outworks of the defensive system—namely, the solitary or lymphoid glands, deal with the infection "*in situ*" more succesfully, and metastasis only occurs when they fail. The first line of lymphatic glands come into action ; now metastasis is the rule. The ovaries or liver are attacked *in the rear*. The reason that suggests itself is, that the mucous membrane of the former organs is fortified with abundant lymphoid follicles, while the tongue at its tip, the nipple, and the skin are not provided with any.

Once these outworks have been pierced or penetrated the physiological process of defence becomes a pathological one.

Let us compare the two well-known conditions of *acute diffuse sepitc peritonitis* and that known as *acute diffuse septic cellulitis*, the *sequela* of an extensive scalding of the skin, by viewing the relationship of the lymphatic system, in regard to the extra corporeal environment of the body, in connection with its mechanism of defence, as shown in these diagrams. Figs. 22 and 24.[20]

In the former condition, the highly toxic as well as toxin generating micro-organisms, have accidentally found themselves within "the hollow square," the peritoneal surface; here there is no possible way of dealing with them physiologically and therefore effectively. What is the result? Again, in the latter case, similarly a condition is produced resulting in extensive sudden destruction of an enormous extent of the lymphatic reticulum, with its sensory nerves, and the whole surface is flooded over with *blood plasma*, rendering it hopelessly defenceless against, if not highly favourable to, the highly toxic and toxin generating micro-organisms, which, until then, had been effectually debarred from penetrating this surface, and surviving. They find themselves within "the hollow square," where there is no possible way of dealing with them *en masse* physiologically. What again is the result? In the secondary toxæmia of variola by staphylococci the same occurs. Need I cite such conditions as Tetanus, Hydrophobia, Tubercular Meningitis, Sleeping Sickness, or Cerebro-spinal Meningitis, *et hoc genus omne*, in order to impress the reader with the feeble lymphatic defence of this all-important ectodermic structure, *the cerebro-spinal system*? In these what also is the result?

Let me here mention incidentally with respect to the lymphatics that if, from any cause, the pre-natal matrices do not develop *at their proper time*, or are otherwise in defect in the cerebro-spinal system, we have the condition that may be termed *infantile lymphatism* in early life and the rarer condition of *adult lymphatism* at this later period.[21] Again, it is well known that the bone marrow is least of all provided with lymphatics. Here we have the red and the white marrow; and, in regard to infections, the former may be looked upon as better off than the latter, which is most remote, as well as encased in bone, though it is supposed to be the cradle of the myelocytes and is termed lymphoid tissue by V. Noorden.

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[20] Charrin (Archives de Phys, 1896), introduced into an isolated loop of intestine bacterial toxins and showed that they rapidly lost their toxic properties, although their direct injection into the portal vein was followed by poisonous symptoms. After destruction of the mucous membrane and its glands by heat or by the action of tannic acid they lost none of their toxic powers when introduced into the intestinal loop. He also found that the toxic symptoms consequent on an infection of the contents of the ileum into a vein could be inhibited by a previous administration of an extract of the mucous membrane of the bowel.

[21] See *Lancet*, February 9th, 1907. "The Role of the blood plasma in disease," p. 376. Dr. Harry Campbell's reference to Dr. Paul Ehrlich, "Studies in Immunity."

But the site where the lymphatic supply may be said to be conspicuously the weakest is the endothelial lining of the arterial and venous systems. This fact, if borne in mind, may throw some light on purely blood infections, the sequelæ of traumatism, as in insect bites and wounds of these vessels. The blood circulation is otherwise inaccessible to foreign microbic life. If it were possible to evoke a leucocytic response on the occurrence of a blood infection in the usual way, it is conceivable that the arteries and veins would become suddenly blocked by the access of leucocytes, and with serious consequences.

The provision for dealing with such an infection is, therefore, entirely different; depending upon the nature of the micro-organisms. The phagocytes which are normally concerned with the katabolic processes, and which pass in and out of the capillaries, deal with them in the ordinary way, when the micro-organisms arrive at parts sufficiently narrow, where the flow of blood is diminished in velocity, chiefly in the spleen, the liver and the kidneys. They may also deal with them within the auricles and the valves of the heart as in the various forms of septic endocarditis. This would occur during the inter-systolic stasis in that organ, where the blood frictional area is greater than at any other part of its course. In these localities antibodies may similarly be formed, at what might be termed the extreme end, and in one sense the wrong end, of the lymphatic system. The resultant chemical substance of the physiological degeneration or clasmatosis of the leucocytes being incomplete, it is not so useful for purposes of sensitization, and varying negative phases in the opsonic index occur. Thus we have the characteristic malaria like pyrexial charts in septic endocarditis.

Further, in this condition there may be evoked a segregating response, by virtue of the hormones, and this at those points where these micro-organisms become *extra vascular*, (1) their emergence from the filamental capillaries, or (2) by their conveyance thither by the leucocytes themselves. We then have produced the condition of cirrhosis of the spleen and liver, and of such organs as are involved, and this pathological condition interferes temporarily with their functions. But in due course the katabolic phagocytes proceed to remove the segregating cells and tissues, and during this process we may occasionally have a relapse, if this process occurs too early. In these blood infections, for obvious reasons lymphatic glandular involvement does not occur, and, in fact, is conspicuous by its absence.

When micro-organisms thus gain entrance into the circulating blood and there cease to exist, they are enveloped in the fibrin and form minute emboli, which become sequestrated in remote, out-of-the-way parts, within the capillary structures of the arterioles, becoming infarcts, or they are "incinerated" in the liver, the resulting product appearing in the bile of the gall bladder for extrusion into the intestine.

Again, when this traumatic infection occurs in the regions extra-vascular to the blood capillaries in the inter-cellular spaces, the micro-organisms find themselves in the extra-vascular plasma or within the lymphatic reticulum; the processes are then, conceivably, influenced chiefly by the hormones, which are necessarily much slower and entirely local, but as a rule most effective. Their failure here may perhaps account for the condition known as elephantiasis and such allied conditions.

But I have wandered greatly from the subject in hand.

If we look back to the history of medicine in Jenner's day, when the sciences of bacteriology and histology had no existence, and when that of chemistry was in its early infancy, we find that the subject of bodily immunity to disease at that time began to be surmised, as it was first observed and practically applied in China.

In spite of their limited powers of investigation, from lack of physical knowledge and suitable appliances, observation and experience led to the adoption of vaccination on a purely emperical basis. The opinions of eminent authorities were freely and insistently expressed in opposition to one another, with unedifying results. The human and bovine economy were considered totally different to one another in every possible respect, as this was before the days of Darwin. The bovine vaccinia was therefore considered to be totally different from the human manifestation of the same, just as we now argue in regard to bovine and human tuberculosis.

The fact of the communicability of the disease from one to the other was perfectly clear and generally admitted, yet no micro-organism was ever suspected as being the causal factor.

> New Times demand new measures and new men;
> The world advances and in time outgrows
> The laws that in our fathers' days were best.

Perhaps it was as well that this was so, or they may have suspended the development and adoption of vaccination till the present day, as it is only very recently that the spore bearing coccus of variola has been identified. The difficulty in doing so earlier may in part be ascribed to the rapidity with which the bio-chemical action between the protozoal pathogenic cell and the bodily cells takes place, when once these come in contact with one another. The invariable result we know is the ultimate destruction of the invading cell and the chemical formation of a potent enzyme after the destruction by physiological degeneration of some of the bodily cells.

The vaccine or lymph of cowpox is a nascent enzyme, which is the chemical resultant of the cellular action between two enzyme containing micro-organisms, such as the spore bearing coccus of variola on the one hand, and that of the leucocyte on the other. It is therefore an enzyme differing from that in either of the cells, from the inter-action of which it originated, but bearing the characters of the enzyme of the more powerful cell to which it becomes chemically and congenially related. It is now more opposed to the enzyme of the less powerful cell and after a certain stage this power becomes attenuated. When this lymph or enzyme is placed in contact with the broken muco-cutaneous surface, it therefore evokes less active and more gradual responses of defence than the original virus from which it arose, and it is dealt with in a somewhat similar fashion as that of the original virus. This results in the production of an enzyme chemically further removed in its composition to that of the original virus, and more nearly related to the enzyme of the leucocyte till it is finally lost. Whereupon the individual concerned requires a re-infection with this particular enzyme or vaccine in order that his bodily cells may re-acquire the characters of defence, which they have in course of time acquired and then lost. It is conceivable that this enzyme under certain conditions is everlasting and undecomposable until brought into contact with another more potent enzyme-containing living cell, but this cannot be the case with the cells or cocci which produced it, unless these are kept so as to vegetate on a suitable medium.

The object of Phagacytosis.

(5). The undoubted answer to the last question is—the acquirement of bodily immunity. An anti-body only results in the survivor of two opposed cells, or two opposed enzymes, such as is in the phagocyte and in the microbe, when the latter is physiologically digested by the former, or when the vaccine, enzyme, or toxin, is physiologically digested by the leucocyte or lymphoid cells. This is effected in the vaccine vesicle of vaccinia *in situ* in which case the enclosed "lymph" is known to contain the antibody in concentration.

The chain of causation involved in these processes appears to the writer to be as follows :—

PHYSIOLOGICAL.—Sensation, gland reflex, vaso-dilator reflex. Hyperæmia, at least at two points, namely, the site of the original stimulus and at the correlated lymphatic gland; generation of leucocytes; leucocytosis; chemiotaxis or exalted metabolism; extra vascular phagocytosis; clasmatosis; vaccine formation, sensitization of plasma (first the extra vascular and then the intra vascular plasma); restoration of the plasmic equilibrium. Immunity.

PATHOLOGICAL.—Absence of normal sensation; vaso-dilator reflex; inco-ordinate hyperæmia, probably at one point alone, namely, site of stimulus at periphery; excessive hyperæmia; gland reflex; leucocytosis; exalted chemiotaxis; segregation *ad lib.* Hyperplasia, which is usually slow; toxæmia, which is usually rapid; according to the peculiar properties of the microbes concerned, that is to say, toxic or non-toxic, or the degree of those qualities

> that they possess. We must also bear in mind the fact of their influence on one another. where they happen to be present in association with the normal flora and fauna of the peripheral surface of the body—intestinal or skin. The chemical neutralization of exogenetic toxins in excess requiring more subtle processes than the plasma is capable of generating (I refer to the extra vascular plasma), their elimination cannot be brought about—the result is death.

Professor Adami, of Montreal (on "The Dominance of the Nucleus"), discusses the physiology and pathology of the nucleus. His views of this highly complex subject are so interesting that I will take the liberty of quoting them freely in this reference. Regarding the finer changes which take place in the nucleus during the course of cell activities, he says:—"If I am not mistaken, it was a native of what we regard as the youngest of the great civilized countries of the world, Professor Ogata, who first in 1883 clearly recognized the finer nuclear changes associated with secretory activity. He called attention to the granules or plasmosomes appearing in the nucleus at the beginning of secretory activity—granules which take on the characters of nucleoli and pass from the nucleus into the cell body. In these he held that the zymogen granules are developed which eventually become (part of) the protoplasm of the cell."[22]

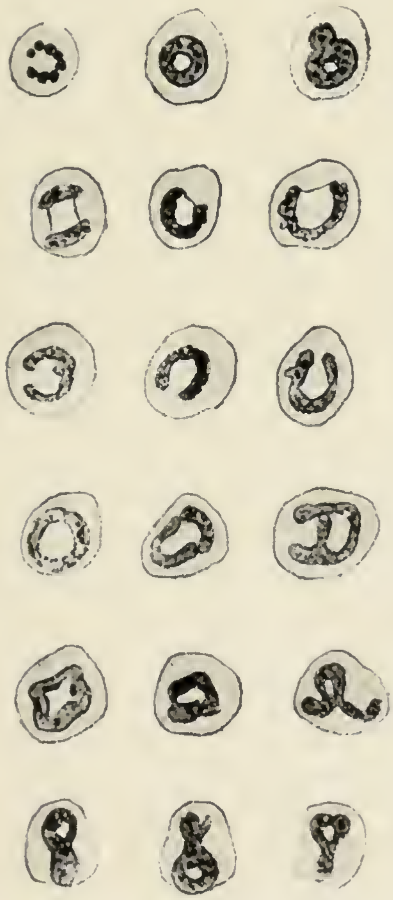

FIG. 23.—Leucocytes undergoing nuclear physiological degenerative changes. (Delamere).

Again, after further observations, he says:—"But clearly the indications are that the higher syntheses, those associated with growth, and those governing the specific enzyme actions of the different forms of cell (i.e., animal and vegetable), are determined and initiated by the nuclear matter." (See Fig. 4, a, b, c.) As to the nucleus in pathological conditions of the organisms, he says:—"Associated with degenerative changes and rapidly growing tumours we may encounter the development of paranuclear bodies (Nebenkerne), sometimes of large size and modified staining properties, lying in the cytoplasm and clearly derived from the nuclear matter. Beyond this statement it is difficult to arrive at any other conclusion than that there is an intimate relationship between these nuclear vagaries and the abnormal cell growth seen in malignant tumours." He further refers to pyknosis and karyolysis or complete disappearance of the chromatin, as evidences of post-mortem conditions in the cells. He is of the opinion that these changes represent exaggerated conditions of normal processes, from the earlier stages of which these cells may recover. In regard to the ferment actions of the cell and their relationship to nuclear activity, he says:—"Referring to the discharge of plasmosomes or spherules of nuclear matter into the cell body, it may now be asked, What chemical processes do these indicate? It is suggestive that under normal conditions this discharge has been noted in cells affording specific secretions, and in abnormal conditions accompanied by the accumulation in the cell body of modified paraplasmic granules or globules." He further enters into the highly complex chemical composition of these. He lays stress on the lecithins, after tracing their origin, and says that these are bodies having remarkable properties, both chemical and physical; they have great powers of holding other substances in solution, and this is true of all the myelin bodies.[23] Thus lipoids of the nature of the lecithins afford us the necessary linkage bodies between various albumens and between albuminous and fatty acids. The mucins would seem to represent a parallel group of carbohydrate proteid compounds; indeed, in goblet cells, according to Steinhaus, there is a total conversion of the old nucleus of the cell into mucinogen. The figures given by this observer are of the same order as those afforded by Ewing of nuclear changes in epithelial cells in connection with vaccinia and variola." He concludes his remarks on "The Dominance of the Nucleus" by saying that it is to the nucleus and its alterations that the chemist and physicist, anatomist and physiologist, pathologist and physician, must apply himself for the fullest intimate grasp of the succession of changes that take place in health as also in disease.

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[22] *British Medical Journal*, December 22nd, 1906.

"Myself when young did eagerly frequent
Doctor and Saint, and heard great Argument
About it and about; but evermore
Came out by the same Door as in I went
There was a Door to which I found no Key:
There was a Veil past which I could not see."

I wish, however, to put in a plea for greater precision in technique in regard to bacteriological research, and also especially in regard to the inoculations of "vaccines," or standardized emulsions of micro-organisms.

Surely we might give up, as coarse and unscientific, the use of such an injecting instrument as the hypodermic needle!

I refer to the microscopic contiguity to the body surface of the reticular tissues which are pre-eminently concerned with bodily defence, namely, the capillary lymphatic plexus, that underlies the external layer of epidermic cells on the one hand and those of the mucous membrane on the other.

A cellular view of the body as represented by a semi-solid multicellular sphere will perhaps lead to the better apprehension of my remarks. We have the sufrace of this sphere uniformly covered with a continuous unbroken coating of cells, representing the skin of the body and the mucous membrane--this cellular coating serves to demarcate the extra-corporeal, environmental sphere, from the intra-corporeal multicellular organic sphere. The merest abrasion on the surface, in a microscopic sense, suffices to bring into operation, so to speak, the "bayonet points" of organic defence, at this part of the immediately underlying lymphatic reticulum, which most minutely and uniformly encases the entire body surface, though internal to the outlying cells mentioned above.

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[23] The therapeutic action of chloroform on the brain cells in *adult lymphatism* may find some explanation here. See Dr. Henry Campbell on "The Role of the Plasma in disease."

It ought to be our aim and intention to obtain an exact physiological reaction, by introducing into this and no other region of the organism such potent medicaments, which are necessarily used in most minute quantities.

In using a hypodermic needle of any known make this cannot be achieved without overshooting the mark, and

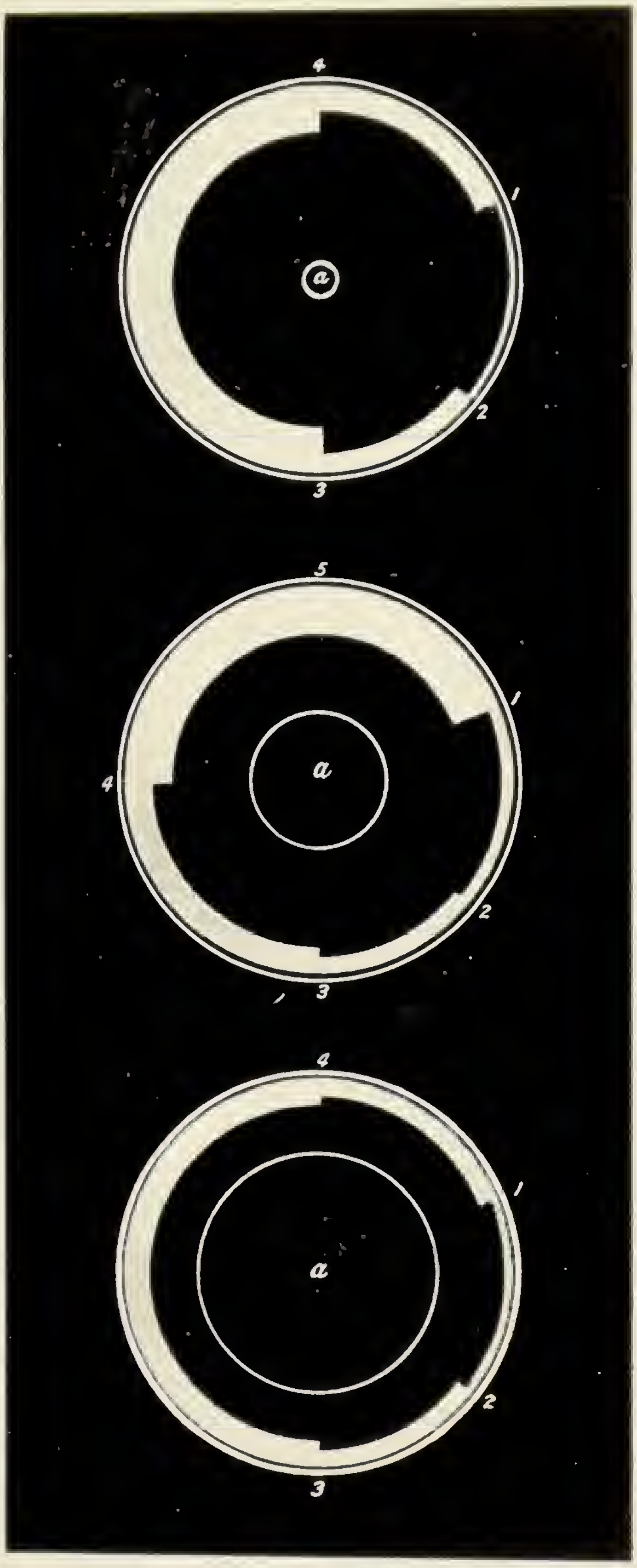

FIG. 24.—Diagrams representing apportionment of lymphatic substance in relation to impregnability of bodily structures at different periods of life. Showing accession of immunity at the expense of the loss of lymphatic substance during these periods. Figures from above downwards in infancy, adult age, and the prime of life. Regions 1 to 2, Skin; 1 to 4, Respiratory surface; 4 to 3, Intestinal surface; 3 to 2, Uro-genital surface. In middle figure 5 to 4 Upper intestinal, and 4 to 3 lower intestinal tract.
(a) Index of immunity.

penetrating the intercellular tissues beyond. Violence is thus done to the blood capillaries, and many sources of fallacy arise, and the more so when, as is sometimes done, the peritoneal sac of the animal is penetrated. These remarks do not apply to the injection of anti-toxic sera, which are vicariously elaborated, so long as we bear in mind the fact, pointed out by Sir A. E. Wright, that some of these manufactured sera are really "vaccines in disguise," and to these the same caution should apply. We have recently read of "mouth immunization," also of the introduction per anum of certain sera, *on to the mucous surface*, and of the success thus acheived. This is because of the greater accessibility of the lymphatic reticulum through these surfaces, there actions naturally being more physiologically obtained. Again, in ordinary vaccination, "cœteris paribus," we get the best results where no blood is drawn by the scarification of the skin and for similar reasons.[24] It is an interesting fact that the Chinese, who were the original inventors of inoculation for smallpox, some thousands of years ago, adopted the procedure of depositing, with an elongated finger nail, the moistened variolous matter *on to the nasal mucous membrane*, in order to bring about the necessary physiological reaction . . . . and they succeeded.

In this reference an abstract in the "Edinburgh Medical Journal," February 1907, p. 189, is significant. In their third memoire dealing with the intestinal origin of pulmonary tuberculosis Calmette and Guérin (Ann. de l' Inst. Pasteur Paris, tome XX No. 8) adduce evidence in support of the view that pulmonary tuberculosis is due to the entrance of virulent tubercle bacilli by the digestive tract and not to inhalation. They consider that two conclusions of a practical nature are evolved from the experiments. "The first is that by carefully avoiding the introduction of tubercle bacilli into the digestive tract, we ought to be able to considerably reduce, if not totally suppress (*sic*) the causes of infection, since it is much easier to guard against the ingestion of contaminated food by bacilli of either human or bovine origin than it is to avoid the inhalation of infected dust. The second conclusion, which is one of very considerable interest and importance, is that an animal given in a single meal a small quantity of virulent tubercle bacilli, finely divided, certainly contracts tuberculosis, either pulmonary or exclusively glandular, or pulmonary and glandular at the same time. It re-acts to tuberculin for from one to two months and sometimes longer, and is yet *curable*. It ceases to re-act to tuberculin when the lesions are completely cicatrised. They point out that as a result, animals so *cured* are not susceptible at least for a certain time to reinfection, even when they are made to ingest much more considerable quantities of virulent tubercle bacilli. They are as it were, *vaccinated*. On the other hand, animals which have undergone two or more successive reinfections by the digestive tract at short intervals never recover. Their lesions become aggravated and go on rapidly to caseation. These facts, the authors consider, explain the frequency with which there are found post mortem in animals killed in the slaughter house, and in human subjects accidentally killed or dying from other causes, tuberculous lesions perfectly cured. These animals and persons have been sufficiently rarely infected with tuberculosis in the course of their existence to have had time for their primary lesions to be cured and so to become *vaccinated*. A large number of animals and persons on the other hand, have become and remained tuberculous because they have undergone a series of successive reinfections before the lesions produced by their first attack were cured.

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[24] "Good marks" are more often the result of mixed vaccination and local or extraneous staphylococcic or streptococcic inocculation, which, though often harmless, is nearly impossible to prevent.

From their work Calmette and Guérin are accordingly led to direct their researches in the direction of obtaining vaccinal immunity against tuberculosis by introducing into the lymphatic system by the digestive tube (which they consider the normal path of infection) tubercle bacilli, attenuated, modified, or deprived of virulence."

I cannot agree with these eminent workers that the intestinal tract is 'the normal path of infection," whatever this may mean. It is most probable that we acquire infection *and I may add immunity*, more by this path in infancy; hence *tabes mesenterica*, which is benign, compared with *tubercular meningitis*, when this occurs at so early a period of life.* But in youth and in adult life, where immunity has not yet been duly acquired earlier, *the respiratory path* is the common channel of infection, during this, and the succeeding period of life. Tuberculosis in the nature of things, can never be suppressed, but it can be appropriately regulated to our needs, by the conference of immunity, and the sooner tuberculin is given up as a diagnostic agent the better. I refer to the method adopted of using it as such.

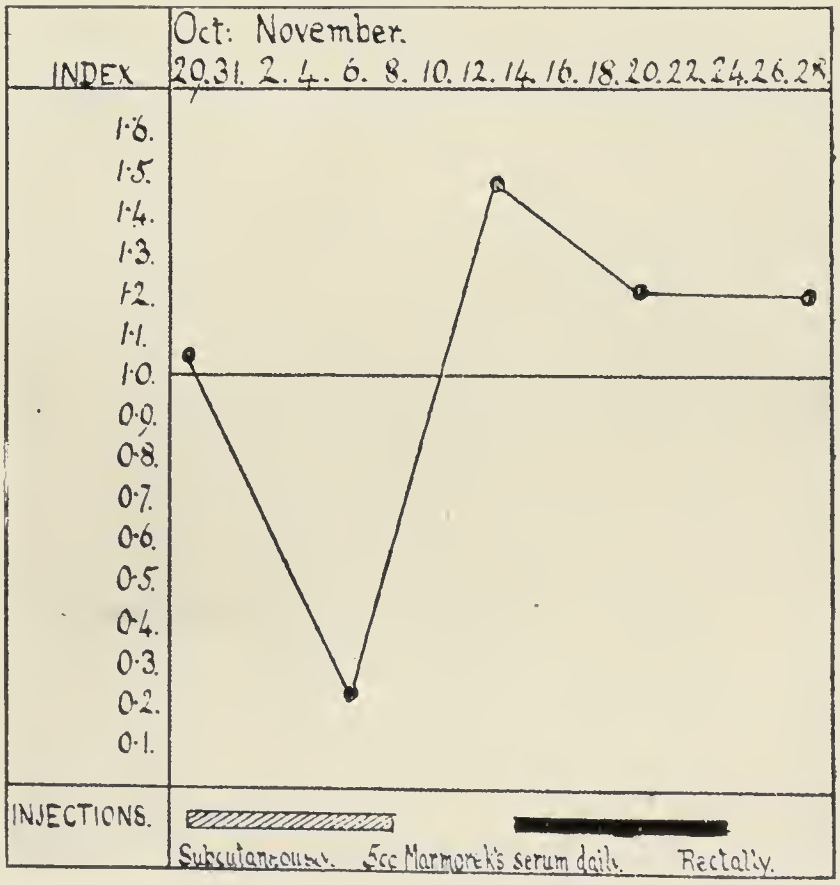

FIG. 25.—Chart. Tuberculo-opsonic.

But the strongest example that can be given in support of the plea I have raised, has appeared in the "British Medical Journal" of the 13th April, since this paper was written; I will, therefore, with all deference to the authors, quote the case, which is illustrated by a tuberculo-opsonic chart verbatim as follows:—

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* See British Medical Journal, 8th June, 1907, p. 1360. Case of Tuberculous Meningitis in boy treated with Tuberculin: Recovery, Recurrence and death.

CASE V.

"T. H. S., a man of 49, was admitted from tuberculosis of the right upper lobe and of both lobes on the left side; he also had tuberculous laryngitis. His temperature was persistently above normal, but seldom reached 100° F. He suffered from much pain in the throat. With a view to testing the effect of serum on this symptom he received subcutaneous injections of serum from October 29th to November 8th. *These were discontinued owing to a fall in the opsonic index.*[25] The pain diminished somewhat during the treatment. From November 14th to 24th rectal injections were administered. Again the pain seemed to lessen, but there was no change in the physical signs. The patient finally left the Hospital unimproved. The number of opsonic estimations in this case was rather small, *but subcutaneous injections of serum produced an alarming fall in the opsonic index;* when the injections were stopped the index soon rose again, but was not affected either way when serum was given daily by the rectum."

The above paragraph speaks for itself, and comment is unnecessary. Marmorek's serum, as has been stated, is one of those to which the term "a vaccine in disguise" would be applicable; yet I do not entertain the least doubt as to its efficacy, when it is intelligently administered—that is to say, *on to the mucous surface*—and no where else, or the consequences will be worse than alarming.

"If men could be satisfied with pure knowledge, the extreme precision with which, in these days, a sufferer may be told what is happening and what is likely to happen, even in the most recondite parts of his bodily frame, should be as satisfactory to the patient as it is to the scientific bacteriologist who gives him the information. But I am afraid it is not; even the practising physician, while no wise underestimating the regulative value of accurate diagnosis, must often lament that so much of his knowledge rather prevents him from doing wrong than helps him to do right.

A scorner of physic once said that nature and disease may be compared to two men fighting, the doctor to a blind man with a club, who strikes into the melée, sometimes hitting the disease and sometimes hitting nature.

The matter is not mended if you suppose the blind man's hearing to be so acute that he can register every phase of the struggle and pretty clearly predict how it will end. He had better not meddle at all, until his eyes are opened—until he can see the exact position of the antagonists, and make sure of the effect of his blows.

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[25] The italics are mine.

But that which it behoves the physician to see, not, indeed, with his bodily eye, but with clear intellectual vision, is a process, and the chain of causation involved in that process."—(Huxley: "The Connection between the Biological Sciences and Medicine.")

Adverting to "the popular discoveries in physiology," Dr. Alfred Russel Wallace says, in his "Wonderful Century":—"Just as we saw how, physically, dust was so important that not only much of the beauty of Nature, but the very habitability of our globe, depended upon it, so we now find that the most minute and most abundant of all organisms are those on which both our means of life and our preservation from death are dependent. For these minute bacteria of various kinds are present everywhere—in the air, in the water, in the soil under our feet. They are, in fact, omnipresent, and under normal conditions they are wholly beneficial." What do we understand by "normal conditions"?

However, with this weighty statement Science should be, and is, in absolute accord. But we civilized nations create our especial environments, and thereby bring into existence pestiferous conditions which the more intelligent of us strive to correct by artificial, and to some extent unnatural, sanitary regulations. For we make sterile streets unlike country roads; there is neither "humus" nor "fertile" dust. On these sterile and "defenceless" surfaces we expectorate, and the myriads of bacteria in a square inch, under the most adverse conditions, proliferate and fructify, returning in due course through the air to other hosts, and so test their resisting powers to microbic invasion. Therefore, it follows that the necessity arises for our constitutions to become adapted to such environmental influences, and in doing so, those only manifest diseases, who have not previously become precisely adapted to that special environment, and have thus acquired immunity. The creation of environment therefore results in the cycle of the creation of life and the maintenance of life and the destruction of life. This is the Law of Environment. (*See interpretation of final Sanskrit quotation on last page*).

Dr. Wallace is content to discuss the *occurrence* and *recurrence* of disease in accordance with the "*doctrine of averages.*"

Professor Carveth Read says, in his "Metaphysics of Nature":—Aristotle admits Chance amongt the principles of things, and irreducible accidentia amongst the consequences. "Opinion and belief Epicurus traced to the persistence of perceptions in the mind, and therefore held that, to be trustworthy, they too must be distinct and verifiable by the senses. Even the atoms, since they are not severally perceptible, can only be the object of belief, and they come under the rule that 'concerning things imperceptible it is necessary to draw inferences from the phenomena.' This is the way of analogy, and it implies a belief in the uniformity of Nature. It also implies that perception is our authority not only for particular sensations, but also for their relations or synthesis; and that the synthesis of belief must also be derived from the perceived connection of things. The only definite synthetic principle discoverable in Epicureanism is the maxim that 'nothing arises from nothing or perishes into nothingness.' And this is now recognized as one of the constituents of the law of Causation." Hence in a scientific sense there is no dirt, no pollution, and, for the matter of that, no death—these being merely chemical transformations, which produce their relative effects. But what we are concerned with is the attainment of positive knowledge only so far as it touches human interests.

SUMMARY.

"'The merit of a theory,' it has been recently said, 'consists not in being true, for no theories are true, but in being fertile'—that is to say, in being not only a satisfactory and self-consistent representation of the totality of the facts, so far as we know them, but also in suggesting by the images used the direction in which to seek for further knowledge. And a theory can only be fertile, one would imagine, in virtue of bearing, in however a remote degree, some resemblance to the truth."[26]

The theory I wish to put forward is based upon the following truths:—

(1). The truth that the power of vital resistance or immunity to an infectious disease can be acquired, and is acquired, only by the appropriate environmental exposure of the individual to such[27] minute doses of the particular infection (or to its particular enzyme properly standardized), and in such a way, that the following dis-ease is more often entirely "latent," so that subjective or objective evidence of it, by any of our well known methods of eliciting these, are not of the least avail. [28] [29]

From this argument it is a legitimate inference, and independent of any hypothesis as to the nature of these infectious micro-organisms, that an immunizing agent or antibody is formed within the organism of the individual. It is the more necessary to distinguish between proved truths which are an abiding possession, and the more or less ephemeral theories based upon those truths, because physicians now look upon theories of any kind as little else than convenient tools.

(2). The truth that lymphatic glandular involvement occurs in all extrinsic micro-organic bacterial diseases. In the great majority of these complaints there need not always be, and more often is not, evidence of such involvement, as this depends upon the extent and virulence of the infection at the time on the one hand and upon the previously acquired, or unacquired degree of resistance of that particular individual to the specific infection in question on the other.

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[26] XIX.—XX. Zimmern.

[27] Report Royal Com. Tuberculosis, 1907.

[28] British Medical Journal. Dec. 15th, 1907, p. 1,686. Edmund Owen on Cancer. The question arises as to what there was in those mice or in that happy individual which enabled the natural forces to vanquish the disease.

[29] British Medical Journal. 1st Dec., 1906. Dr. G. H. A. Clowes. British Medical Journal. Dr. Bashford. Royal Cancer Research Fund.

(3). The truth that the antibody or vaccine in the case of two such well-known infectious diseases as Tuberculosis and Plague—namely, that originated by the Bacillus of Tuberculosis and that by the Bacillus Pestis in the animal organism, has been extracted and isolated from the so called diseased lymphatic glands, after survival from the bodily infection; and further that this substance has recently been put to practical use and found to effect remarkable cures by producing the condition known as bodily immunity to these infections.[30 31 32]

(4). The truth that Phagocytosis of bacilli in these infections is now recognised as being brought about in response to their stimuli evoking the mechanism of bodily defence, which takes place under certain conditions, namely the presence of a due amount of opsonins, of sufficient incitor elements and the required number of phagocytic leucocytes.

It becomes necessary to place in their proper sequence and bring into due relation the last two truths, and in attempting to do so I have ventured to resort to a principle which has produced great results in modern research namely, that it is worth while to seek elsewhere for what is known to exist anywhere.

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30 The Lancet. Aug. 25th, 1906. Dr. Peter Paterson. (Obs on sterile caseous matter.

31 The Lancet. Jan. 26th, 1907. Dr. Mallanah. (Lmphatic gland extract in plague).

Ibid. Mr. McCulloch. "The Induction of Autovaccination, etc."

32 The Lancet. 23rd Feb., 1907. "Tuberculosis Cured or Immunized."

NOTE.—An abstract appearing in the British Medical Journal of the 18th May, 1907, re "Climatic Bubos," is worth mentioning, as it concludes with the plausible statement that "The two cases described add to the evidence against an immediate microbic origin, and do not in any respect justify the pestis minor hypothesis."

P. G. WOOLLEY (Archiv fur Schiffs und Trop. Hyg., Bd. xi., Heft 2) reports on two cases of climatic bubos occurring in the Philippine Islands. The clinical history, the histological changes, the results of culture experiments and of animal experiments were similar in the two cases. In the clinical examination no evidence was given of malaria, syphilis, or gonorrhoea, nor was there any visible lesion on the lower extremity drained by the glands. The bacteriologist reported that stained smears made from the fresh glands showed nothing resembling bacteria, protozoa, yeasts, or moulds; no growth took place when cultures were made on 1 agar slants, and kept under aerobic conditions for two weeks. An emulsion was made from one of the softened glands and injected subcutaneously into a guinea-pig. Two months later the animal was killed, and nothing abnormal was noted at the autopsy. The glands themselves were enlarged and in most cases firm. Upon section they were seen to be pale and looking as if they were more or less simply hyperplastic. Some of them showed areas of necrosis, with little tendency to softening, but rather to caseation. Some had undergone softening, and these showed no bacteria and no protozoal intracellular or extracellular bodies. The chief change in the tissue of the affected glands was an endothelial hyperplasia with areas of fibrino-purulent exudation and coagulation necrosis. These latter areas contained, in addition to polymorphonuclear leucocytes and fibrin, a considerable number of macrophages.

Within these cells were remnants of ingested cellular material, much of it in the shape of round bodies of sizes varying from 0.5 to 1.5 microns, which stained intensely with magenta. These bodies were only found in necrobiotic areas. The author, after careful consideration, decided that the intracellular bodies did not show constant enough characteristics in the various cells to be considered organisms, and that they were partially degenerated cellular material ; certainly they had no constant likeness to the bodies of Leishman. A brief review of the different theories of causation of the disease is made in the article. The two cases described add to the evidence against an immediate microbic origin, and do not in any respect justify the pestis minor hypothesis.

Such a statement seems to the writer to be very weak scientifically, even if it is not calculated to restrict sound investigation.

On a par with the above is the following answer to a correspondent, " Inquirer," appearing in the British Medical Journal of the 1st June :— " Strumous " Glands. " Surgeons act rightly in removing " strumous " glands, because these generally contain tubercle bacilli, and might if left *in situ*, give rise to disseminated tuberculosis. It is true that there are many people in excellent health who had enlarged crevical glands when children, but it has not been satisfactorily proved that their general health and their freedom from any subsequent manifestations of tuberculosis are attributable to this circumstance. At the same time it is possible, as has been shown by experiment that a healed tuberculous focus may confer a certain amount of active immunity. There is therefore nothing unreasonable in the theory that a healed tuberculous adenitis may be credited with some protective influence. According to this view the gland would not merely act " mechanically " or locally as a trap for the arrest and destruction of tubercle bacilli but would increase the general capacity of the organism for resisting infection."

PART II.

The Circling of the Central Problem of Cancer.

After studying the Cancer Problem as presented in the Bradshaw Lectures of 1903 and 1907 one is led to the belief that we must look to the histologist or to the bacteriologist as having gone "farthest north" in the required direction before we may know that for which search has, for so long, been strenuously made.

It is with trepidation that I venture to express some views which are not quite in accord with the theories that certain admitted masters and leaders in the Profession of Medicine have hitherto put forward, and which they hold. But the words and exhortations of Mr. Edmund Owen in his Bradshaw Lecture of this year are both encouraging and inspiring, for he says :—"In reviewing these various methods it would ill become the most conservative of us to condemn, or to stand upright and stiff in the temple of Æsculapius, and with self-satisfied look express smug thanks that we are not under the influence of such ruthless surgical activity." And again :—"In the world of therapeutics there are still dark tracts and continents which can be discovered only by men of imagination and energy."

Recent speculations on the subject of cancer do not all start from a common point. Two of the chief of these attempts to solve the problem have been made, one from the point of view of the bacteriologist, and the other, from that of the histologist ; while that of the anatomist, of the physiologist or of the chemist, has found little or no place, to say nothing of the embryologist and comparative physiologist. The bacteriological views are based on the extrinsic origin of the disease, while the histological views are based on its intrinsic or entogenous origin.

In this year's Hunterian Oration Mr. Butlin referred to the basis of surgery in Hunter's day, and clearly showed that everything was then given up to anatomy, and "anatomy was studied rather for its direct service to the individual surgeon than with the belief that it might prove of great use to the art, if it were studied from a wider point of view. Biology, physiology, physics, chemistry, pathology had no place in the education of the surgeon, and those few persons who ventured—as some advanced thinkers did—to maintain that a knowledge of physiology and pathology was desirable in a medical man, were for the most part treated with contempt or were left to preach unheeded." He further very aptly compared the surgery of the eighteenth century with navigation before the use of the mariner's compass, which, by the way, originally came from China.

He says :—" The mariners of those days went down to the sea in ships and accomplished voyages often difficult and dangerous, under the guidance of the stars by night and of well-known marks by day. They carried them through, not once, but again and again, successfully, and with a marvellous confidence begotten of experience and observation. So did the surgeon, guided by similar observation and experience, carry his patients through sickness and operation so often and so surely that there could be no better guides than he, and his fathers before him, were accustomed to rely on."

Now we have the causal agents of an infection on the one hand and the resultant of their chemical activities upon the phagocyte on the other, namely, the immunizing agent, or what, for the want of a better term, we may call the vaccine. This substance is brought into existence in consequence of the exertion of the cellular mechanism of bodily defence. The cell which survives the attack in successfully meeting it, acquires the power to resist all similar attacks, its vitality being thus prolonged in that particular environment.

In the light of recent clinical knowledge it seems to me that the time has now come when in the diseases which involve the production of an immunizing agent, we may safely adopt as a fundamental working hypothesis, that of the implication in these diseases of a microbic causation. That is to say, a microbic invasion necessarily involves, at least the initiation of the formative process of an immunizing agent, this process being completely carried out in those cases, in which the disease is successfully repelled.

It is highly probable that in the great majority of these, this lymphatic glandular involvement is, in its earliest stages, physiological, and therefore not manifested to our senses; particularly in those common conditions in which we have obvious pathological glandular involvement. But it is everywhere said, that the lymphatic glands are the weak spots in the human economy ; and their involvement is looked upon most unfavourably, as a source of danger, both by the physician and the surgeon.

When the vast potentialities of the lymphatic system in the human economy become known, I venture to predict that a similar advance will have been made upon the surgery of to-day, as was made by Harvey in his day and generation.

With permission, I will again quote from Mr. Butlin's masterly oration, with some modifications :—" In truth the surgery of the present day is composed of a vast unwieldy mass of observation and experience balanced on a single point, the study of morbid histology ; it is like some great logan stone, which even the weakest force might rock and a violent shock might overthrow. No wonder that, under these circumstances, opinions on vital questions of physiological chemistry do waver. ! "

I hope to show that the lymphatic system and its glands are the most resistant parts of the economy, and that it is to them that we owe the "vis medicatrix naturæ." In truth it may, in a certain sense, be looked upon as having hydra-headed resources. That intrinsic disease of the lymphatic glands is extremely rare is generally admitted ; and we also know that the cells which these glands generate are most resistant, and it would be difficult to estimate their age. These cells have been found alive and active in the human body many hours after death (Delamere). Further, it would seem to be a fundamental fact in nature that no form of unicellular organic life is known to exist, that can engulf and digest the living human phagocyte in its own natural environment, unless it be the phagocyte itself. Hence the marvellous vitality and survival through the ages of the ancestral leucocyte.

This function of devouring and digesting unicellular organisms is one that can be traced in the Protozoa, more particularly in the sub-division of the nucleated forms (Monera and Endoplastica). In the Protomyxa, which are the primitively independent myxopods, these unite into plasmodia, which is the first indication of agglutination and also of the phenomenon of segregation, in the function of defence. The process of digestion by the phagocyte depends upon certain factors, which need not be here entered upon. If we analyse the phenomenon of phagocytosis in a microbic invasion, we have the causal agent containing its enzyme or toxin brought into immediate contact with the phagocyte which contains its enzyme or cytase. The resulting chemical substance is said to be effected by catalysis or fermentation, whereby a dissociation and rearrangement of their constituent chemical molecules takes place, within the phagocyte. This substance is probably a more highly organized enzyme, which becomes the immunizing agent, against that particular infection. But in certain peculiar infections of the animal body it happens that a chain of processes is necessary, before the immunizing agent can be formed ; and this I have attempted to describe in the early part of this paper.

It will be obvious that the chemical change set up between the enzymes of two micro-organic cells cannot be strictly compared with that which takes place between an enzyme containing organism, such as yeast, when it acts upon a dead organic substance like grape sugar, which is of much simpler chemical composition. It is true that here Alcohol and CO_2 are formed, and that these are inimical to the yeast organism, and kill them. This action is known in chemistry as a "reducing action," and their death may be accounted for by the Environmental Law, from overcrowding.[33]

Granting, the constant correlation of the causal agent with the corresponding immunizing agent, in all diseases of microbic origin we are at liberty to infer from the acknowledged presence of one of these two factors, the existence of the other; that is to say, the existence of a microbic infection, from the presence of the immunizing agent. To take some of the commoner infections, where we have lymphatic glandular involvement :—CA = causal agent I = immunizing agent.

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[33] See Dr. A. L. Gillespie's "Natural History of Digestion." Ferments and Ferment action Contemporary science series.

1	2	3	4	5	6
Tuberculosis	Syphilis	Leprosy	Measles	Scarlatina	Typhoid
CA	?	CA	CA	?	CA
I	I	I	I	I	I

7	8	9	10	11	12
Rheumatism	Plague	Variola	Cancer	Acne	Diptheria
CA	CA	?	?	CA	CA
I	I	I	I	I	I

On this principle I venture to predict, that in the case of the diseases numbered 2, 5, 9 and 10 future investigation will enable us to fill up the gaps. For my own part, I believe that these gaps have all, been already filled up, more especially in regard to cancer.

I have discussed elsewhere the role of the phagocyte in producing the specific vaccines, or immunizing agents; and I have indicated the conditions under which segregation and metastasis occur, describing also the sequelæ of those pathological conditions which follow upon inco-ordination of the normal processes of defence. I quoted the experiments of Drs. Peter Paterson and Mallanah, in regard to their extraction of the immunizing agent in Tuberculosis and in Plague respectively, from the diseased lymphatic glands. In regard to the presence in the animal body of an immunizing agent in cancer, I am now able to quote Drs. Bashford and Clowes (of London and New York respectively), as well as Mr. Edmund Owen himself, as stating that its presence in the human body has, on some few occasions, been proved, "though this is of very rare occurrence."[23] Now it happens that, on the occurrence or application of a continued series of stimuli at certain points of the external periphery under varying conditions, the sensory responses evoked vary accordingly, and that this responsive function, which is actuated by the nervous system, depends, among other factors, upon the age of the individual, as regards its effectiveness. In order to adequately comprehend the exquisite delicacy of these bodily perceptions, which probably transcend the grosser 'sensory perceptions,' let me refer the reader to an article by Huxley "On sensation and the unity of structure of sensiferous organs," in "The Nineteenth Century," Vol. V., April, 1879, pp. 597-611.

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[23] British Medical Journal. Bradshaw Lecture, 1907.

"The impressions of the sense of touch on which we chiefly have to rely for the diagnosis of these growths are less definite and less easily conveyed than the impressions of the eye. The microscope has here, too, given its surprises, and many a surgeon has received a report on a breast tumour from the laboratory for which his clinical examination had not prepared him. The rule which has at present to be followed is, always to suspect cancer when a swelling in the breast is not obviously of some other nature, and to go to the microscope for a decision."[24]

Such is the deplorable state of our knowledge and of our resources! So that when a surgeon is brought face to face with a doubtful "swelling" of the breast, his plight may be compared to that of the Russian Admiral when he was off the Dogger Bank not so long ago. This state of affairs is not mended by Dr. Dawson Williams' further exhortation, when he says :—" It is well to have clearly recognised that the text book signs of cancer are all severally useless for the diagnosis of an early malignant growth."[25]

To revert to the individual : first and foremost, what is the state of his lymphatic system and its glands ? We know that these are highly developed and are very active in infancy, when they chiefly correspond to the intestinal tract, and that they are less in evidence at the more protected parts of the body. As age advances they diminish in some parts and increase in other parts, for instance, along the respiratory tract ; and so they vary during different periods of life, new ones being formed in place of those that have completed their functions in the bodily wear and tear. But, apart from these, there are many which come into being independently at various sites or matrices. These sites are pre-natal, and remain the essential parts of the lymphatic system, predestined, in the course of bodily growth and development, to be connected up with the general scheme of the system in the normal manner in which these structures come into being. They continue in a dormant state to preserve their embryonic anatomical characters until the causes arise which rouse them into growth, in order to meet the environmental requirements of the individual ; just as do the cells which undergo differentiation in other parts of the frame, as is actually witnessed in the growth of the teeth, bones, skin and its appendages, the larynx, the mammæ and the organs of generation. (See Fig. 24.)

It is conceivable that, if at these transition periods, a rare form of microbic infection occurs on the external periphery, the responses evoked are not of the most effective or efficient kind, and that whatever responses are evoked, the sequences of the processes of defence are not so physiologically effected. Hence the inception of a morbid process in the tissues concerned, especially in early life. Of this there may or may not be any evidence, either subjective or objective. Yet profound changes may have taken place, for example, phagocytosis alone, or this to a less degree, together with segregation to a greater degree in varying degrees of effectiveness, thus producing a tumour or tumours. Beyond an opsonic examination of the blood, we have absolutely no means of investigating or diagnosing the condition with certainty in these initial stages, or even much later, unless we are able to detect the early cytolytic changes in the epithilial cells at the inception of the precancerous stage of the lesion.

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[24] & [25] British Medical Journal, 26th May, 1906, Editorial.

" Precancerous is a term which has long been in use to describe certain pathological conditions which have been regarded as leading up to carcinoma, but as not actually carcinomatous. Mr. Butlin's observations prove that, in regard to cancer of the tongue, at any rate, the term has been to a considerable extent erroneously employed, in that some of these so-called precancerous lesions are in reality actual malignant growths."[26]

These developing lymphatic glands cannot be looked upon as rudimentary or embryonic organs, although when physiologically mature they are capable of generating rudimentary as well as highly organized tissues, even the gametogenetic tissues of the testes, in order to meet special emergencies, where required. It is easier for them to produce in such emergencies the less organized tissues than those of more highly organized glands or nerve structures. In regard to the products of these activities it is therefore often difficult to distinguish microscopically between normal and abnormal tissues when they are of the simple " all pervading " connective tissue or fibroid tissue types. " Fœtal rests " and " embryonic vestiges," the former being the result of aberrant embryonic cell mitosis, come under quite another category ; and these doubtless account for the presence of dermoid tumours and cysts in after life.

In phylogenesis, as in ontogenesis, these clasmocytic cells exist before the appearance of the hæmatopœitic organs. Leucopœisis, like hæmatopœisis, appears to be an elaboration of many stages, varying according to the zoological species and according to the age of the individual. In a given animal and in a given region the quantity of lymphatic glandular substance is not always the same ; in fact, it is greater at the less protected parts ; and it may be added, that for purposes of prolonging their vitality, in their respective environmental spheres, those animals which exist in close relationship with micro-organic life have proportionately more lymphatic substance than those which do not. For example, birds are known to have lymphatic glands in the cervical region alone ; and, according to Budge, lymphatic dilatations, or hearts, are present in the embryo of the chick, but they disappear with the development of the allantois. In mammals, although the lymphatic hearts disappear entirely, they are still represented by the innumerable expansions above the valves, in the course of the more elaborate lymphatic ducts. Their mode of origin in the fœtus and throughout life is important to consider. "They do so by buds, or islands, which are absolutely closed cul-de-sacs, and this long before any glands have appeared. From the first the trunks are distinguishable from their capillaries. The former very soon show their valves, and develop from buds which are originally full. The latter spring from buds originally hollow, and having no valves.

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[26] British Medical Journal, Vol. I, 1906.

The initial lymphatic growth is sometimes followed by involution phenomena, which have been studied by Ranvier in the epiploon of the new-born kitten. In some cases the lymph is retained by a pair of valves whose action is reversed; in others closed, elongated, or pointed vesicles are seen, which represent portions of the lymphatic system that have become isolated in consequence of the atrophy of the intermediate segments. This may account for the origin of certain cystic formations in after life." (Delamere). The close functional relationship of the reproductive glands, namely, the ovary and the testis, with the somatic as well as gametogenetic lymphatic gland, is one that should be borne in mind; and it is interesting to here mention the fact that in the Bryozæ and in some of the Polychetæ the lymphogenous and the reproductive glands, which are so distinct in the vertebrates, are blended into what Cunéo has styled the lympho-sexual glands. But, it may be said: This is all very well; what about the great feature which distinguishes carcinoma from all infective diseases, that is, its property of producing secondary deposits which reproduce the structural details of the organ or tissue primarily affected? This is of extremely easy explanation, if what I have previously stated be borne in mind, namely, that it is easier for the lymphatic glands to generate and to despatch cells to form the simpler tissues than those for specialized tissues. When a microbic invasion is being responded to, there is local structural damage, and therefore need of immediate repair of the 'fixed' tissues; and the two processes become concurrent. On the occurrence of a metastasis, at the outset, those cells intended for the primary repair become diverted in the altered chemiotaxis to the secondary deposit, till such time as fresh responses are evoked, by subsequent damage to the tissue in question. As the tendency for re-co-ordination of function becomes established; repair is delayed, according to the complexity and organization of that particular tissue. Meanwhile the simplest tissue is substituted, to be removed later, and in due course, after immunity has been acquired, as is the case in spindle-celled sarcomata. But where the plasmic equilibrium (if I may invent such a phrase) is not in a state of "rest"—

"The best laid schemes of mice and men
Gang aft aglee."

This does not take place in the secondary deposits of the other torpid infectious diseases, seeing that the microbes concerned in them are more toxic than cytolytic, as is the case with the microbe of cancer ; and this fact is also evidence in support of its peculiar protozoal origin. If in the eminently cytolytic destruction which follows ; the element of toxicity be introduced, by a supervening attack of erysipelas, or the toxin of some such microbe as that of the *Bacillus Prodigiosus* be administered, this loss of balance in the concurrent processes is at once restored and made more co-ordinate. We have precisely the same phenomena in an attack of *Cholera morbus*, when practically, an extravasating hemorrhage takes place, a violent irritant like capsicum or black pepper would seem to be contra-indicated, yet it is these drugs that are widely given in an epidemic in the Tropics ; and they simply restore the equilibrium, by their toxic stimuli. I have in such cases observed the remarkable effects of a wine-glassful of Lea and Perrin's sauce ; and there are many who will bear me out in this statement. Arsenic and other such "Cancer cures" act similarly.

Further, in the case of the cancer microbe, the lymphatic glands concerned in the reparative processes are impressed with the facts of its rapid permeation, and the imminent devastation of the soft entodermic structures, and these are anticipated by the glands which are functionally concerned.

"Metastasis is a complicated subject, but *we know* (*sic*), *at any rate, a considerable amount about lymphatic extension.*" If I may venture to say so, this statement is scientifically and terminologically inexact. It also savours of a degree of self-satisfaction that, under the circumstances, is not warranted. The ordinary reader must on reading such a statement involuntarily exclaim, in the words of Truthful James :—

Do I sleep ? Do I dream ?
Do I wander and doubt ?
Are things what they seem ?
Or is visions about ?

For, in truth, what do we know about lymphatic extension ? The following picture, though it has its points, cannot be said to be very convincing to the thoughtful :—" In this way the ovaries may be fairly pictured in the mind, receiving a light covering of falling cancer cells, as evergreen shrubs are clothed by snowflakes in winter.'[27]

In regard to the parasite itself, which seems to be so elusive, if not delusive, it is conceivable that it has the property of *selecting the weakest points* in the periphery, at the transitional regions of the peripheral epithelial cells, which need not be enumerated, as this region has been termed the " cancer belt." But such regions are accidentally produced by long absence of physiological stimuli, by traumatism, heat and by certain chemical irritants, which result in cutting off these structurally defective regions, from the central nervous system, by a sort of induced local sensory pareisis; lasting for indefinite periods. From these tissues the necessary responses of defence cannot be effectively evoked, and here these microbes are enabled to establish a footing, and to proliferate; and they subsequently interfere with the functions of the body, when they come in contact with healthy tissue. Here they are dealt with in the manner described, according to the degree of their virulence and their extent of penetration. I am therefore led to conclude that no exciting cause will produce cancer or sarcoma, in the absence of the peculiar stimuli applied accidentally, and primarily at some point or points at the periphery of the body, thus bringing into cellular contact with it, minute micro-organic cells of ectogenous origin, when and where, the bodily mechanism of defence is, from a variety of causes, plasmic or otherwise, debarred from responding to these said stimuli, in the manner required. In other words, so as to effectively bring about the formation physiologically, in the individual, of the vaccine or immunizing agent, whereby his bodily cells and plasma acquire tolerance to the consequent altered environmental conditions. This is brought about by the presence of these most minute forms of cell life, which do exist. Just as no amount of injury will of itself excite suppuration without the presence of pathogenic or pyogenic micro-organisms in the injured tissues, so no amount of injury will give rise to a tumour without the presence of these micro-organisms (which are bound to exist).

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[27] British Medical Journal, Vol. 1, 1906. The italics are mine.

As to the "recurrence" and "malignancy" of these neoplasms, the *a priori* explanation would be that the feeble defensive powers that might have been accruing to the tissues surrounding the neoplasm or growth, by the transudation into them of the previously elaborated vaccine, now within the glands of the diseased mass, is further weakened by the extirpation of this mass. But there is the further probability of the entire removal of both sound and unsound lymphatic glands, as well as that of a fair margin of healthy tissue, advisedly done—

> "We but teach
> Bloody instructions which being taught return
> To plague the inventor."

There is a probability—indeed, there is frequent evidence—of re-infection in the surgical wound, and *in the event of remnant metastases*, under such circumstances, the "malignancy" is naturally greater, as will appear obvious, if there be any truth in what has been stated. But there is a further explanation and not less important factor in regard to recurrence. When, by the surgical removal of a very large mass of tissue, the stimulus for effecting the necessary repair is set up, immediately on the return of consciousness after the effects of the anæsthetic, this stimulus is so profound that the condition known as "shock" is produced, and this is always anticipated and prepared for by the surgeon. Under other circumstances, the result of a less severe stimulus of this kind, reparative responses are more co-ordinately evoked from the nearest correlated lymphatic glands, and it is possible that the entire lymphatic glands of the trunk may be called upon to contribute to the reparative processes thus made necessary. Under these circumstances the isolated stimuli of remnant metastases fail to secure the special response necessary for their further segregation. But this may be only partially effected, until at a later period there is a recurrence of the growth, under or near the recently formed scar tissues, which merely serves the purpose of a patch, efficient no doubt, in many ways, but often very crude. The phenomenon of Chemiotaxis is one that is now generally recognized, except that greater stress has been laid upon its partial phase, that is, the positive—the remaining, or negative, portion of the phase is seldom mentioned. It is a fundamental scientific law that when there is "action" this is invariably followed by "reaction." Here we have two oxygenated spheres in the body tissues, both being hyperæmic; between these a path of molecular motion is established, namely, from the glands to the site of the infection, thus establishing a complete circuit or circulation. It is of the essence of a circular motion that, that which moves returns to the place from whence it started; it constitutes an efficient "defense de circuler." It is to this phenomenon that the term lymphatic circulation might appropriately be applied, and not to that flow of the fluid in the lymphatic ducts and vessels. We have evidence of this phenomenon in the protoplasm of the Monera, between the nuclear structure and the cell periphery, when the cell is at rest, as well as in the leucocyte itself. (See Fig. 2, a and b). On this phenomenon Dr. J. O. Wakelin Barrat's researches are highly interesting.

May not it be, that in the "round celled" sarcoma—we have here the most resistant cells to cytolytic action specially developed, mere nuclei so to speak without protoplasm?

In a sarcoma of the large vascular benign variety, it would seem that the spleen, in its close relationship to the lymphatic system, plays an active part in aiding the process of "segregation" alone and on an extensive scale; we here have the further result of inco-ordinate action. I merely offer this as a suggestion which is conceivable, when we consider that the skin occasionally does duty for the kidneys, as an eliminatory organ, though their structural relations could not well be more remote. The manner in which the spleen would effect this would be, by ceasing, *pro tem.*, to draw upon the leucocytic elements for the elaboration of red cells in the blood in order to enable the glands to cope with this condition of greater complexity. Conscious as I am of many imperfections, I have contributed my mite towards the dissipation of what I believe is a widespread surgical delusion in regard to the functions of the Lymphatic system.

I have before me the last edition of the admirable treatise on "Tumours; innocent and malignant," by Dr. Bland Sutton.

In this work he includes an account of the prevailing but irreconcilable opinions held by competent men in regard to the origin of cancer, and he impartially sets forth in these pages those of the numerous hypotheses that are worthy of consideration, namely : (1) The Embryonic; (2) The Parasitic ; (3), The Biologic. If I may say so, each and all of these hypotheses seem to me to be something more than mere guesses at the truth. In fact they *are* true, everyone of them, *if taken together*, but none of them are true alone.

Cohnheim's " rests " retain potential powers of growth because they are the predestined sites of lymphatic tissue development, which necessarily remain dormant during certain periods of life ; but their sudden active " growth " only occurs, with the provocation which it has not been possible to observe hitherto. The provocator is the protozoon of cancer, and the biological phenomena of cell mitosis has its cradle in the lymphatic glands and nowhere else. That is to say that the phases of mitosis which the cells from the lymphatic gland undergo, depend entirely upon the *impress*, which is imparted to them, when they are yet leucoblasts within the germinal areas of the gland, this area being internal to the gland follicles. But we can no more support these theories by concrete evidence, than we could demonstrate the fact of a human ovum developing into a male or female of its species, previous to its further embryonic development. The Biologic theory arises out of Cohnheim's theory and may be said to constitute an extension of it. The kaleidoscopic changes of the leucocyte under varying plasmic conditions are such as to baffle description, and can hardly be conjectured, as evidenced by the excellent demonstrations of cytologic transformations, made by Farmer Moore and Walker in relation to nuclear division.

It is natural that we should find these peculiar nuclear changes more at the centrifugal periphery of the growth—" situated in a zone behind the growing edge of the advancing neoplasm."

Why should there be any doubt on the point, that the cells in a cancerous, or any other growth, are actually formed from the histogenic cells of the body ? In order to adequately meet the effects of such microbes as those of cancer efficiently it becomes necessary for such histogenic cells to be produced, as can withstand their cytolytic powers. That is, in that particular region, where the primary infection occurs. This form of fixed cell, may be one that has no existence in the body tissues, hence the difficulty in its elaboration. May not the " archoplasmic vesicle " be a lytic stage of the protoplasmic degeneration of the leucoyte ?

It is said that the strongest argument against the parasitic theory is the failure to cultivate the cancer microbe outside the body. If this is all, surely the outlook is highly promising. There was this difficulty in regard to the *diplococcus rheumaticus*, now happily overcome ;

and in this remote part of the 'kingdom' we have been able to get some satisfactory opsonic indices to it, lately. There is news that the *entamœba hystolytica vel dysenteriæ*, has at last been successfully cultivated outside the body, and I believe that the protozoon of cancer will also be so produced in due course. But if the men of Jenner's time disputed about the microbe of variola, had they the microscopes we have, as well as the laboratory conveniences; had they gone in pursuit of this protozoon, pending the treatment by vaccine, of variola, what the result might have been is beyond conjecture. They intuitively proceeded, led by observation and experience to empirically use, and adopt, natures methods of conferring immunity, and I think it behoves us to do the same, though perhaps less empirically and more scientifically.

The doubts which Mr. Henry Morris has expressed regarding the insufficiency ot Cohnheim's "embryonic theory" when he said, "Obviously Cohnheim's doctrine is insufficient by itself to explain the formation of malignant new growths—in scar tissue, in unabsorbed inflammatory products, and in parts after injuries and operations ot various kinds "[28] —are such as I hope. have been supported in this paper.

Among the above worthy theories Dr. Bland Sutton has however, by some curious oversight, omitted to mention what to my mind is the most important of all of them, namely, that which has been described as "the ingenious theory" of Mr. G. Lenthal Cheatle. In my humble opinion, his has been the most brilliant piece of scientific work in this direction yet achieved. It bears the stamp of being strictly anatomical as well as physiological. The credit for which he modestly attributes to Drs. Head and Sherrington.

I refer to the substance of the two papers read by him before the Pathological Society of London in 1903, entitled, "The Behaviour of Cancer within Nerve and Trophic Areas." In this paper he concludes by saying: "I have shown that the spread and limitation of cancer in the skin and muscles bear a marked relationship to the presence of nerves, and the absence of nerves where normally they previously existed bears a marked relation to the limitation of cancer. But I cannot say whether cancer can genetically arise in a completely denervated area. I know this disease (rodent ulcer) can exist for a considerable time in a completely denervated area, although it does not spread in that area."

The vital generation of enzymes within the cells and tissues is admitted and is intelligible, *but this is not so with regard to the de novo vital origin of a new form of parasitic cell within the cell or the cell tissues*, as a consequence of the most subtle chemical activities, the so-called cancer cell. I merely mention this for what it may be worth.

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[28] British Medical Journal, Dec. 12th, 1903. Bradshaw Lecture, 1903.

I do frankly admit that these are all hypotheses, but they are the hypotheses which seem best to throw light upon and to harmonize with the data we possess regarding the function and the relative importance of the lymphatic system and its plasma respectively. Nay, more, it is in harmony with what we know concerning the very lowest forms of life and their defensive mechanisms.[29] I feel I shall have done some service if I have demonstrated the dominance of the leucocyte and impressed the reader with the conviction that the future will see, not merely a hæmatological but a plasmic pathology and physiology. From the "*omnis morbus ex humoribus*" of our predecessors to the "*omnis morbus ex sanguine*" of the modern student of serums, we see surely before us the conclusion, "*Omnis morbus ex plasmate corporis ex auctoritate Jenneris*," if not the "*Omne biophorum ex biophoro ejusdem generis*."

Professor Huxley in his address at the International Medical Congress at York, said :—

"Seeing that the actions called 'vital' are, so far as we have any means of knowing, nothing but changes of place of particles of matter, we look to molecular physics to achieve the analysis of the living protoplasm itself into a molecular mechanism. Living matter differs from other matter in degree and not in kind ; the microcosm repeats the macrocosm : and one chain of causation connects the nebulous original of suns and planetary systems with the protoplasmic foundation of life and organization. From this point of view pathology is the analogue of the theory of perturbations in astronomy, and therapeutics resolves itself into the discovery of the means by which a system of forces competent to eliminate any given perturbation, may be introduced into the economy. It will in short become possible to introduce into the economy a molecular mechanism which, like a very cunningly contrived torpedo, shall find its way to some particular group of living elements, and cause an explosion among them, leaving the rest untouched."

This remarkable prediction has already been fulfilled thanks to Sir William Crookes and to Professor Roentgen. And to those of my readers who are interested in this subject, let me refer them to a paper contributed to the Archives of the Roentgen Ray, which appeared in April's issue of that Journal. The molecular instability in the cells of all emergently repaired tissues and, neoplasms is thus easily "exploded," while the more symmetrical molecular stability of the "fixed" tissues, serves to protect them undisturbed.

Having no rivals to criticise (in fact, there were none on the Himalayas), I have no need to expend energy on the many theories and more doctrines that do exist. The one I have put forward includes those that have prevailed, and I am led to conclude :—

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[29] "The digestive power of the amoebæ is their chief defence from their enemies, and by it they are able to protect themselves and to obtain their food at one and the same time." Dr. A. L. Gillespie, "The Natural History of Digestion."

1.—That cancer incidence in the human body is of ectogenous source, and therefore extrinsic, and in accord with the Law of Environment and that of bodily defence.

2.—That the causal agent is most probably a non-toxic protozoal form of cell life, with peculiarly powerful cytolytic enzymic effect, analogous to amylolytic and proteolytic properties.

3.—That the mechanism of bodily defence is evoked in this, as in all other noxious infections.

4.—That it is only capable of infecting an individual who has immature, or atrophied " lines of defence," or other long-standing peripheral muco-cutraneous defect.

5.—That the responses that are evoked in consequence are, as a rule, more often inefficient to repel it.

6.—That the plan of action is the same as in other tissue infections, except that it is in accord with the exigencies of the subject's bodily needs.

7.—That the peculiar feature of secondary metastasis in cancer, is therefore owing to the devastation of the fixed tissue elements primarily affected ; thus influencing the anabolic processes of repair, concurrently with the katabolic processes of opposing the protozoon during exalted metabolism.

8.—That a " vaccine " to cancer is formed in the lymphatic glands themselves, at a very early period of their involvement, they are then probably not perceptible.

9.—That there is reason to hope that by proper culture, and introduction to the lencocyte, a vaccine or perfect remedial agent, vicariously prepared in a living animal, will be possible ; when the functions of the lymphatic system are duly apprehended.

Hermann Lotze, the great Medical Metaphysician of Göttingen, has said : " A hypothesis must limit itself to asserting what is possible, that is to say, what can be conceived or pictured as matter-of-fact. Our procedure may be logically correct without being endorsed by reality. Suppose we have selected our hypothesis and are trying to deduce from it the original appearance, we may find that our deductions do not agree with the data, either because our analysis of the latter was defective, or because fresh observations, which were impossible before, have brought out new aspects of the thing. In that case the hypothesis must needs be amended. This may be done in two ways. The hypothesis contains elements which in themselves admit of being modified, and we determine these in a more suitable manner, so that as grounds for the deduction of the given fact are no longer either too wide or too narrow, but just adequate. The other way is to add on fresh subsidiary hypotheses in regard to a few of its leading features. If we look at the way in which the body of science has grown up historically, we see that it, too, is very willing to essay new points of view under old and incommodious forms, if only not to loose any of the truths which have once been won through these forms. I do not mean to say that science should or will rest content with such methods ; we all trust that the result of all our painful investigations may prove a simple and thoroughly consistent whole ; but until we have arrived at that result we must not be deterred by the oddly complex and patchwork garb, in which our views needs be clothed, if we are careful to adjust them to each freshly known feature of our object by means of subsidiary hypothesis tacked on to our earlier assumptions in regard to it.

This is the only way in which we can hope to reach the simple and plain result we seek. The more carefully we now proceed, the more surely may we expect that in the cause of our procedure our Manifold assumptions will spontaneously reduce themselves to simpler and more universal ones, so that in spite of all the circuitous reasonings employed, a net result will remain with us which is not only simple and synoptical, but completely covers every part of our postulate. In conclusion, all will admit that a lucky gift of insight may make us able to do without all these roundabout methods; but logic cannot impart inspiration—the only method it can teach is what we have cited. Nothing can warrant our assuming by way of hypothesis a circle, which is at the same time a triangle; it is beyond the constructive power of our fancy to raise a mental image of such a figure, nor could it ever present itself to our senses as a given matter of fact. On the other hand, we may assume the existence of invisibly small yet extended atoms of unchangeable shape and size; there is no contradiction in the notion of them, which would prevent our conceiving them as possible objects of perception, were our senses rendered more acute by artificial means. We may probably have to modify this idea, when we try to think it out and examine its possibility as an element in the system of Nature; but still there is no need to do so till we have availed ourselves of it as a preliminary principle and found it of permanent use in accounting for particular phenomena.

I submit what seem to me to be better working hypotheses, as incentives to sound scientific work. If in dong so I have contributed my mite towards the dissipation of what I believe is a widespread surgical delusion, in regard to the functions of the lymphatic system an important object will have been attained.

Interpretation of the Sanskrit Quotation.

(From the Vishnupurana.)

The Creation,—*all created things and beings.—is brought into existence by* **Brahmâ,** *under whose divine form the* **Supreme** *is manifest as the* **Source** *and the* **Cause of All.**

The **Supreme** *as maintaining the* **Creation** *in its divinely originated existence has the manifested form that is known as* **Viṣṇu** (*Vishnu*)*; and as causing the transformation of all created things obeys, by the way of this destruction of their manifested forms, the* **Supreme,** *who appears under the attributes of* **Siva** (*Shiva*). *The* **Bhagavän** *is the synthesis of the* **Three Divine Persons,** *of which they are the manifestations in relation to the Universe of created forms.*

But the **Unity,** *that makes in truth, but* **One Divine Being,** *of the* **Great Three Manifestations,** *itself also in all* **Creation,** *so that birth and life and death are but a* **ONE,** *even in this the limited field of positive Science: and to so regard the processes of generation, life and death is, I venture to maintain, a fundamental condition for fruitful thought and scientific research.*

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सृष्टिस्थित्यन्तकरणाद्ब्रह्मविष्णुशिवात्मिकाम् ।
स संज्ञां याति भगवानेक एव जनार्दनः ॥

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